The effectiveness of autologous demineralized tooth graft for the bone ridge preservation: a systematic review of the literature

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Resorption of alveolar ridge after tooth extraction often compromises dental implant placement and esthetic. Alveolar ridge preservation is a common procedure performed in order to preserve the pontic site for a prosthetically ideal position. This procedure has already become an indisputable need. Tooth matrix as bone substituted material poses osteoconduction and osteoinduction properties and as autologous graft, this material is free of antigenic reaction. This biomaterial allows the three-dimensional reconstruction of the bone, is easy to prepare and has a low cost. The aim of this review is to summarize and put in evidence the properties of tooth as bone substitute and its use in alveolar ridge preservation.

Bone regeneration continues to be one of the most studied areas by researchers. Although many bone replacement materials have been suggested, autologous bone remains the gold standard in this field (1), but the disadvantages of using autologous bone are well known (morbidity, limited amount that can be taken) and for these reasons it is necessary to use another material that may have these properties but without these limitations (2-6).

One of the most common clinical procedures performed in cranio-maxillofacial is the alveolar ridge preservation. This procedure is applied in order to prevent bone resorption for a later implant procedure ore simply to preserve the pontic site (7). Tan et al. and Ashman et al, concluded that after tooth extraction is expected a bone loss approximately 30-60% in horizontal width after six months and 10-20% in vertical length compared with what was the dimension of bone before extraction and each year the resorption continues at a rate of 0.5 to 0.25 % (8-15). This process is affected by a number of factors, inflammatory response, an irregular vascularisation,

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chronic events and disuse atrophy are the main cause of the alveolar ridge resorption (9, 16-21). The lower jaw is known to be resorbed faster than the upper jaw (22). Clinically these changes especially in the buccal bone are important for the aesthetic areas (23-34). Avila-Ortiz et al., consider the use of biomaterials a necessary procedure to prevent the physiological resorption of the alveolar ridge (35). The tooth material after extraction has always been considered as unnecessary residue, but due to its composition and properties this material is being used more and more (36-42).

The dental matrix contains the inorganic part which consists of hydroxyapatite (*HA)* (43). Between synthetic *HA* and tooth derived *HA* there is no significant different, but tooth matrix is more similar to bone matrix because of the organic component found in it (44). Proteins *(BMPs),* and collagen represent the organic part of tooth matrix. This consistency very similar to alveolar bone is also explained by the fact that they both origin from the neural crest (45-48).

The main criteria of a bone substitute material:

(i) biocompatibility (to osteointegrate without causing inflammatory reactions) (49-53);

(ii) osteoconduction (to serve as a scaffold for cell activities);

(iii) osteoinduction (triggering bio-chemical process so steam cells can differentiate into osteoblasts);

(iv) osteogenesis (formation of new bone matrix) (54-57).

Healing of bone tissue occurs as a result of an interaction between stem cells with immune cells, osteoclasts, and osteoblasts activity. Even if the chronic inflammation may lead to implant failure, the body's inflammatory response is of a particular importance because it activates biochemical signals which bring the immune cells to the region (58). The dental matrix compared to *HA/TC* is shown to be more bioactive and biocompatible (48, 59).

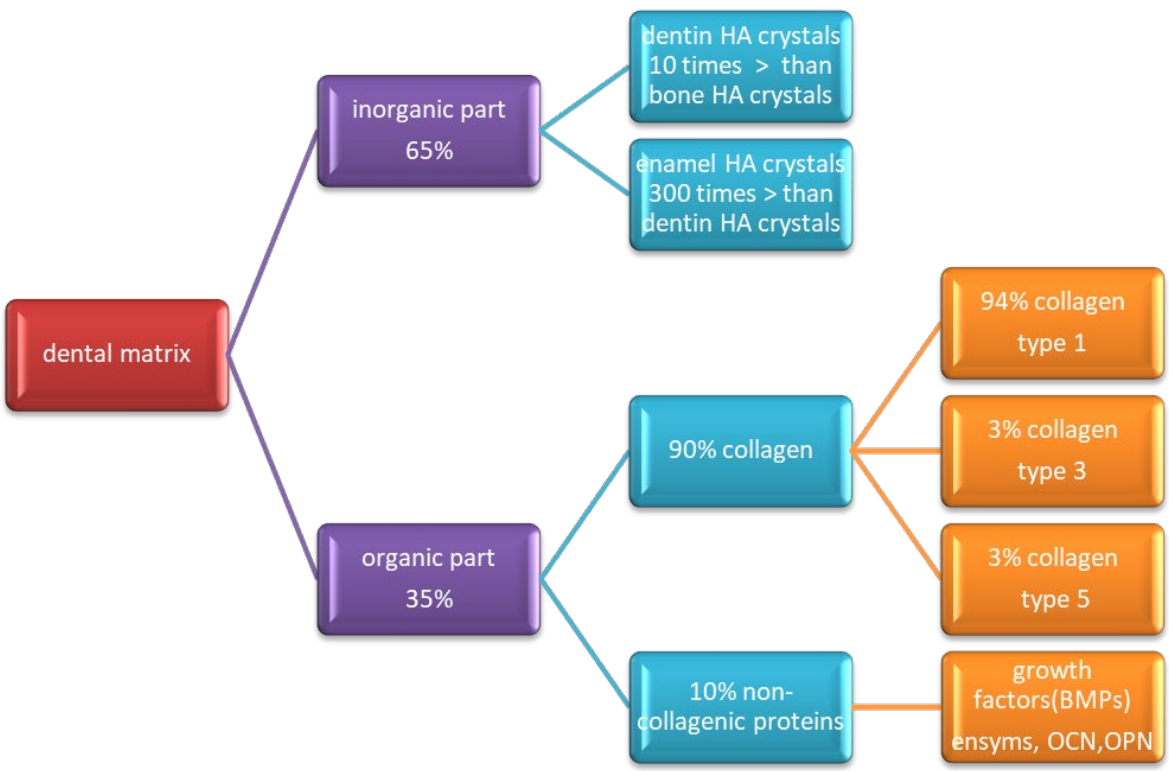

Fig. 1. *Tooth chemical composition: HA- hydroxyapatite, BMPs- bone morphogenetic protein, ONC- osteocalcin and OPN- osteopontin.*

Calcifications of dental matrix from the physiological point of view, is considered as a processes of *HA* production (60).

The ability of tooth derived material to act as a natural scaffold are widely accepted (46, 61, 62). Dentin is composed of 65% inorganic material *HA* $[3Ca_3 (PO4) 2Ca (OH)_2]$. The biggest difference between dentin *HA* and bone *HA* is the size of crystals, bone *HA* crystals are 10 time smaller than those of dentine (48, 63).

The other 35% consists of organic matrix and water. The organic part is composed of 10% of non-collagenic proteins as well as growth factors *(BMPs)* and enzymes, and 90% collagen especially type 1 collagen (48, 63) (Fig. 1).

In biomaterials that are used in bone regeneration, both biophysical and biochemical properties affect cell proliferation and differentiation in order to provide tissue healing (64, 65).

For larger defects, especially more than two centimetres, the use of bio-active molecules is recommended (66, 67). In fact, the third generation of biomaterials used as bone substitute consist in scaffolds which are able to induce cellular response (68, 69). The use of growth factors in combination with biomaterials is believed to develop osteoinductive effects of the scaffold (70), and that their absence can lead even to a non-union of the graft with the host body. In 1991 Bessho et al., observed in the dentin matrix the presence of the bone morphogenic protein *(BMP)* (71, 72). Bone morphogenic proteins *(BMP)* that are part of transforming growth factor family (*TGF*) play an important role in osteogenic differentiation (73).

The aim of this review is to evidence the effectiveness of autologous tooth graft in alveolar ridge preservation summarizing the properties of tooth matrix as bone substitutes.

Table I. *Electronic databases search with Boolean strategy.*

Databases Search strategy	TITLE-ABS-KEY "((Bone grafts OR Bone substitutes); (Bone regeneration AND Scaffold); (Autologous tooth graft); (Dentine graft OR Tooth graft); (Bone morphogenic protein AND Bone regeneration); (Ridge preservation AND Tooth matrix); (Alveolar Ridge Augmentation OR Socket Preservation) Inclusion criteria: study in cranio-maxillo facial, human study, publication of the last five years Exclusion criteria: study in animal, in vivo and ex vivo Databases: PubMed/Medline, PubMed/Central, and Google scholar

Table II. *Summary of the included articles according to the main characteristic of the clinical study: study design, number of sites, patients treated, anatomical region, follow-up.*

Authors	Year	Journal	Study Design	Total sites	Patients	Region	Follow up
Pang et al.	2017	Clin Oral Implants Res	Prospective	33	24	Maxilla/mandible	6 months
Valdec et al.	2017	Int J Implant Dent	Case series	4	4	Maxilla	1 year
del Canto-Diaz et al.	2018	Med Oral	Pilot study	18	9	Maxilla/mandible	16 weeks
Minetti et al.	2019	Appl Sci	Pilot study	34	28	Maxilla/mandible	6 months
Dwivedi et al.	2020	J Oral Biol Craniofac Res	Prospective	30	30	Maxilla/mandible	6 months

MATERIALS AND METHODS

To obtain the needed information for this search we performed a quantitative analysis of the literature in the archives Pubmed-Medline with Boolean strategy. In order to develop this narrative review, the basic articles selected were histological outcomes. After the initial screening of 871 papers a total of 72 papers were included in this review. The search line of keywords and inclusion/exclusion criteria are listed in Table I.

RESULTS

The clinical illustrative studies are all selected with some criteria (they are all study in cranio-maxillofacial, are human studies with the exclusion of animal and *in vitro* or *ex vivo* studies). This study included publications of the last five years (Table II and Table III).

In this review, it was difficult to concentrate the study in randomized controlled trials because there is not much evidence for this subject with RCT articles, that is why we included different studies (pilot studies, case series). Pang et al., in a randomized clinical trial used demineralized dentin matrix in 24 patients. This study concluded that there was no significant difference between dental matrix and *Bio-Oss*® which is a biomaterial widely used in the procedure of ridge preservation considering autogenous demineralized dentin matrix a valid option in this procedure (74). Valdec et al., in 2017 used demineralized autologous tooth graft in ridge preservation and 3-4 months later was proceed with the implant placement.

One year after the prosthetic procedure a loss of 1.1mm in the horizontal dimension and 0.76mm in the vertical dimension was seen. Authors considered autologous tooth a promising material in pre-implantological ridge preservation (75). Del Canto-Diaz et al., in 2018 used autologous dental material combined with collagen membrane for the preservation of the alveolar ridge. Results of this study revealed differences in bone density at 16 weeks between the control group which was not

Table III. *Summary of the included articles according to the characteristic of the clinical study: comparative control, histomorphometric new bone and radiographical bone loss after the healing.*

Authors	Year	Journal	Control	New Bone formation test	New Bone formation Control	Ridge Dimension loss test	Ridge Dimension loss control
Pang et al.	2017	Clin Oral Implants Res	anorganic bovine bone	31.24 ± 13.87%	35.00 ± 19.33%.	Vertical: 5.38 ± 2.65 mm	6.56 ± 3.54
Valdec et al.	2017	Int J Implant Dent	-	-	-	Vertical: 0.76 mm; Horizontal: 1.1 mm	-
del Canto-Diaz et al.	2018	Med Oral	-	-	-	Vertical: 0.42 mm; Horizontal: 0.46 mm	Vertical: 1.77 mm; Horizontal: 1.91 mm
Minetti et al.	2019	Appl Scis	Endodontic treated Tooth	36.68% (±8.90%)	20.78% (±13.29%)	-	-
Dwivedi et al.	2020	J Oral Biol Craniofac Res	-	-	-	Vertical: 0.638 ± 0.75 mm; Horizontal: 0.678± 0.81 mm	-

filled, and the tested group filled with autologous dental raft, control group 922.68 ± 250.82HU and tested group 564.35 ± 288.73HU.

Authors considered autologous dentin graft a promising material in socket preservation technique (76). Minetti et al., evolved a multicenter clinical study in 98 patients using autologous demineralized and granulated tooth graft combined with collagen membrane. After four months 106 implants in total were placed with a follow up of 9 - 45 months. Four months after surgical procedure bone volume was 41.47 ± 11.51%, residual graft was 16.60 ± 7.09% and vital bone was 21.89 ± 9.72%. In conclusion authors declare a real scaffold with osteoinductive properties that preserve bone volume for an adequate implant-prosthetic rehabilitation of the alveolar ridge (77). Dwivediand Kour used autogenous fresh mineralized tooth graft for ridge preservation in a study of 30 patients. The histological analysis revealed 67-100% of bone formation and 34-66% of new bone formation in respectively 60% and 40% of cases. This study considered the side chair autogenous tooth graft a gold standard for ridge preservation (78).

Tooth matrixes preserve bone volume for a long period of time because it has a slow resorption rate (74). Both the width and the length of bone preserve the dimensions with a very low bone loss (48, 75-78). This material offers good osteoconductive (48, 74, 76-78) and osteoinductive properties serving as a biomimetic and bioactive scaffold (48, 77, 78). In ridge augmentation are seen optimal results (48, 74-78) and can be considered an adequate bone substitute in pre-implantological bone preservation (48, 77, 78). As a biomaterial is easy to handle and with a low cost (48, 77, 78).

DISCUSSION

The aim of the present investigation was to evaluate the effectiveness of bone regeneration with autogenous demineralized tooth through a systematic review. The screening and the eligibility assessment of the articles determined a low quantity of papers for a statistical meta-analysis evaluation, while only 1 randomized clinical study was identified from the database search. Moreover, the large heterogenicity of the design of studies could represent a substantial bias for a comparative evaluation. Different materials are suggested in bone regeneration, but very often they present various difficulties and shortcomings in their properties (79-84). An ideal grafting material must bebiocompatible with the host site, osteoconductive/ osteoinductive, and biodegradable. Grafting material must also possess mechanical properties that enable bone volume preservation and surface conditions with porosity that improve angiogenesis, must be of easy handling and with an appropriate cost (85). The dental matrix can be considered an ideal scaffold. The porous micro-structures that this material poses improve blood circulation and promote cell adhesion. The dental matrix has a slow resorption which guarantees the preservation of bone volume by providing correct osteoconduction (48, 74, 76-78, 86, 87). On the other hand, Kabir et al., used dentin graft in critical defect. New bone around the dentin graft was noticed after four months and inside the pores too. This biomaterial showed osteoconductive and osteoinductive properties (88). This fact has been confirmed by other authors in other studies (48, 77, 78).

Autologous dentin grafts eliminate the risk of antigenicity (46, 48). An autologous tooth can be conserved and then used by the patient even after a long time from extraction. The dental matrix preserves the elements without additional liquids. Schmidt-Schultzand Schultz confirm that the tooth preserves both the inorganic and the organic matrix even after hundreds of years (89). For the first time in 1965 Marshall R. Urist hypothesized the existence of these proteins capable of forming ectopic bone (90, 91). Since then, many studies have been focused on this low-molecular weight glycoprotein and its effects on tissue regeneration (48, 71, 92-98). The presence of *BMPs* in reconstructive biomaterials is important for the recruitment and the differentiation of mesenchymal stem cells (*MSCs*) in mature osteoblasts (73, 92, 99) also *BMPs* reduce healing time (98) and stimulate angiogenesis (93, 94). In the large *BMPs* family, *BMP-9* is known as the protein with the highest osteogenic effect. *BMP-9* is capable to stimulate the differentiation of

progenitor cells and to intervene in angiogenesis in order to form new bone even in critical defects (94, 95). Among growth factors *BMP-2* can also be distinguished as one of the strongest stimulants. Its use has reduced the risk of infection and the time of hospitalization. The results obtained by the use of *BMP-2 are* comparable to those of autologous grafts especially in terms of bone density and bone volume (96). Although *BMPs* have a strong osteoinductive potential, this ability is strongly related to the doses that are used (97), because unwanted effects can be obtained from a high dosage (98). Another important fact is that if these proteins are used alone, they lose their properties because they are very soluble. *BMPs* need a carrier to improve bone regeneration and the combination with biomaterials is important (48). In dental matrix the*BMP* is found naturally incorporated in physiological quantities (48, 71). In comparison with other biomaterials autologous tooth very often has provided more satisfactory results in bone regeneration. Differently to tricalcium phosphate *(TCP)* which shows a rapid resorption without maintaining the bone volume, the use of dental matrix preserve bone in length and width after tooth extraction (100). Bovine bone also preserves the volume for a long time as it has a slow resorption (101), the resorption rate of dental matrix is compared to that of bovine bone (102), but in case of a second intervention for the placement of delay implants, there remains the suspicion of implant osteointegration if the surface of implants encounters bovine particles which have not been resorbed (81).

While when the surface of the implant comes in contact with the tooth it does not present problems, tooth material has a friendly approach with implant surface (103); all this brings to the conclusion that dental matrix is a promising material in alveolar ridge preservation (48).

Pohl et al., conducted a study to compare the tooth material used as a block with dentine particles. For the augmentation of the alveolar ridge, 20 patients were enrolled and only tooth block was used in four of them; in seven, dentine particles and in the other patients a mix of tooth block with dentin particles. In this study authors accepted the tooth material as a promising alternative in ridge preservation, but the dentinal block shows a very slow resorption compared to dentine particles. For the tooth block there was no macroscopic signs of bone remodelling and the graft had distinct clear margin from the bone (104).

In another study conducted in animals, Schwarz et al., used autogenous teeth for lateral alveolar ridge augmentation. The teeth were cleaned, the crown of the tooth was cut, and cement was removed. In one group endodontic treatment was done and then the canal was filled with $CaOH_2$. In the other group the tooth was not treated endodontically. Root dentin was used en bloc to fill the bone defect. Bone block was taken in the retromolar region to compare the results obtained from the use of autologous tooth. The authors concluded that the group, which was not treated endodontically, made no difference in ridge augmentation compared to the endodontically treated and filled with $CaOH_2$group. They observed that grafts were reabsorbed to be gradually replaced by homogenous bone with parallel fibres. In this case, for the lateral augmentation of alveolar bone the dentinal block gave good results followed by the later implant placement (105). Becker et al., in the continuation of this experiment, reported that the dental block used as bone graft in comparison with autologous bone showed greater exposure and had a higher failure rate (106). Kim et al., used autogenous tooth block in 22 patients for ridge preservation. This procedure was done in maxilla for 12 patients and mandible for 10 patients and if there was no initial stability for the implant the procedure was delayed for 3-6 months after the first surgical procedure. This study concluded that tooth block gives better result in maxilla compared to mandible, hypothesizing that one of reasons may be the highly vascularised bone of maxilla which helps bone remodelling (107).

The data collected in this study demonstrate that autologous tooth graft preserved the alveolar bone volume after tooth extraction (48, 74-78, 87, 100, 104, 107). This material shows promising histological outcomes with a considered rate of vital bone formed (48, 74-78, 87). Autologous tooth matrix appears to be a good clinical and biological alternative for ridge augmentation that support the implant immediately and delay placement (48, 77, 78, 87). The use of this biomaterial needs further

studies that will determine the way that this material gives its best results.

The chemical structure of tooth matrix makes it possible for this biomaterial to offer structural support and a substrate for new bone deposition. Used as an autologous graft, it is free of disease transmission and antigenic reaction. This study has limitations as more RCT studies are needed in this direction, but within its limitations, we conclude that autologous tooth matrix is a bioactive scaffold which opens new frontiers in bone regeneration. Autologous tooth matrix can be considered a promising material in ridge preservation.

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