Alveolar Ridge Preservation after Tooth Extraction Using Different Bone Graft Materials and Autologous Platelet Concentrates: a Systematic Review

Arturas Stumbras[1], Povilas Kuliesius[2], Gintaras Januzis[1], Gintaras Juodzbalys[1]

[1]Department of Maxillofacial Surgery, Lithuanian University of Health Sciences, Kaunas, Lithuania.
[2]Faculty of Odontology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania.

Corresponding Author:
Arturas Stumbras
Department of Maxillofacial Surgery
Lithuanian University of Health Sciences
Eivenių g. 2, LT-50028, Kaunas
Lithuania
E-mail: arturas.stu@gmail.com

ABSTRACT

Objectives: To review and assess the efficiency of different post extraction socket preservation techniques.
Material and Methods: An electronic literature search was performed on the MEDLINE and Embase databases. The review included human studies published between from January 1st, 2007 to January 1st, 2018, in English. Outcome measures included dimensional changes and/or histological evaluation of alveolar bone.
Results: Twenty-six full text articles were reviewed, 16 of which met the inclusion criteria and were selected for the study. Autogenous tooth graft prevented vertical resorption the most: -0.28 (SD 0.13) mm, observation period (OP): 4 months, while the least effective approach was beta tri-calcium phosphate (β-TCP): -1.72 (SD 0.56) mm, OP: 4 months. Estimating horizontal resorption, the most effective technique was biphasic calcium sulphate (BCS) with β-TCP and hydroxyapatite (HA) - BCS + TCP + HA: 0.03 (SD 2.32) mm, OP: 4 months, while β-TCP was the least efficient: -1.45 (SD 0.4) mm, OP: 4 months. Evaluating residual graft particles (RG) and newly formed bone (NFB) ratio the best results were achieved with demineralized freeze-dried bone allograft: RG: 8.88%, NFB: 38.42%, OP: 5 months, whereas magnesium-enriched hydroxyapatite was least effective: RG: 40.82%, NFB: 31.85%, OP: 4 months.
Conclusions: This review revealed that even though there are numerous types of biomaterials for socket preservation none of them can completely stop alveolar bone loss after tooth extraction. Furthermore, lack of information about qualitative evaluation of bone was noticed indicating that further studies regarding this topic are needed.

Keywords: allografts; alveolar bone loss; biocompatible materials; platelet-rich fibrin; tooth extraction.

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INTRODUCTION

Osseointegration and longevity of implants depend on the quantity and quality of alveolar ridge at the time of implant placement [1]. Teeth extraction is leaded by alveolar bone resorption which rapidly begins and continues for years. Different studies showed that alveolar bone loss during first 12 months after tooth extraction was 11 - 22% of alveolar bone height and 29 - 63% of width while two-thirds of ridge is lost during first 3 months after tooth extraction [2,3]. Thin buccal bone plate causes major alveolar ridge dimensional changes, especially in aesthetic and premolar areas [4,5] while in posterior area of jaws alveolar ridge resorption results in vertical bone height decrease, which requires sinus floor elevation in maxilla and the use of short dental implants or alveolar nerve lateralization in mandible [6,7]. Usually resorption is greater in buccal cortical plate compared to the lingual side [8,9]. Tooth extraction in patients with thin periodontal biotype and buccal bony wall can cause not only dimensional bone changes but also soft tissue recessions [10,11]. The biggest alveolar ridge resorption may occur in cases with teeth affected by periodontal or endodontic pathology, trauma caused tooth loss or aggressive tooth extraction during which a buccal bony wall is fractured [12,13]. Under these circumstances and in absence of bony wall barrier fibrous tissue ingrowths into post extraction socket, impairs alveolar bone regeneration and causes intense resorption of alveolar ridge [14].

To achieve successful implantation and long-term results, three main objectives should be achieved: sufficient bone volume, keratinized gingiva around the implant neck and proper implant position from prosthetic viewpoint. Therefore, it is very important to preserve as much alveolar bone as possible at the time of tooth removal, this way reducing edentulous ridge resorption rate and bone remodelling after tooth extraction [15].

Autogenous bone as bone graft material is still considered as a "gold standard" for bone regeneration, although some limitations, such as extra site of surgery, prolonged time of operation, unpredictable resorption, the risk of donor site complications and limited autologous bone availability from bone graft harvesting techniques [15] motivate the search for alternatives in bone regeneration. Most of bone graft materials possess osteoconductive properties and serve as a scaffold for new bone regeneration. Only demineralized freeze-dried bone allograft (DFDBA) has properties of osteoinduction, but it still varies between each donor and tissue bank [16,17]. As a supplement of bone graft material, platelet concentrates such as platelet-rich-fibrin (PRF) or plasma rich in growth factors (PRGF) could be used. It is known that platelets and leucocytes secrete growth factors which can enrich bone graft material and provide osteoinductive potential [18-20]. This study aims to review the latest information about different biomaterials used for socket preservation and evaluate them in terms of dimensional and histological changes of alveolar bone.

MATERIAL AND METHODS

Focus question

The following focus question was developed according to the problem, intervention, comparison, and outcome (PICO) design (Table 1):

What biomaterials are used for socket preservation after the tooth extraction and which of those show the best results regarding alveolar dimensional changes and quality of newly formed bone?

Types of publication

The review included studies on humans published in the English language. Letters, editorials, PhD theses were excluded.

Table 1. The focus question development according to the PICOS study design

Component	Description
Problem (P)	Bone resorption after tooth extraction
Intervention (I)	Filling alveolar socket with regenerative biomaterial
Comparison (C)	Comparison between efficiency of different biomaterials
Outcome (O)	Different dimensional changes of alveolar bone
Study design (S)	Random controlled trial
Focus question	What biomaterials are used for socket preservation after the tooth extraction and which of those show the best results regarding alveolar dimensional changes and quality of newly formed bone?

Types of studies

The review included *in vivo* (human trials) prospective and retrospective studies, clinical trials, case-control and case series studies published from January 1st, 2007 to January 1st, 2018.

Information sources

The information sources were the MEDLINE (PubMed) and Embase databases.

Population

All age groups were included. *In vivo* studies had to be completed in healthy individuals with no systemic diseases. Subjects in the included studies must have at least two extracted teeth performed with socket preservation technique.

Literature search strategy

Following PRISMA guidelines electronic databases (PubMed, Embase) were searched in order to locate articles concerning the use of all kinds of biomaterials for socket preservation.
The Keywords used for the search included: („socket preservation") AND ((„PRF") OR („PRGF") OR („Xenograft") OR („Biomaterials")). The search was restricted to English language only. Articles published from January 2007 to January 2018 were searched.

Selection of studies

Articles were independently subjected to clear inclusion and exclusion criteria by two reviewers as follows. The reviewers compared decisions and resolved differences through discussion. When consensus could not be reached consultation of a third party was asked. The third party was an experienced senior reviewer. Findings of the articles were studied when they were deemed eligible for inclusion in this paper (Figure 1).

Inclusion and exclusion criteria
Inclusion criteria for the selection

The full text articles with possible relevance were assessed with the following inclusion criteria:
- Study performed with humans only.
- At least one biomaterial available on the market had to be tested.
- Observation period had to be at least two months or more.
- Procedures had to be carried out with healthy people with no systemic diseases.
- Radiographic and/or histological evaluations of alveolar bone changes had to be performed.

Exclusion criteria for the selection

- Not enough information regarding selected topic.
- Case studies.
- No biomaterials used for socket preservation.
- Only clinical evaluation of alveolar bone changes.
- No statistical data.

Sequential search strategy

During initial literature search, all articles were screened and excluded based on titles and abstracts. The following stage of screening involved reading full text articles to evaluate and confirm study's eligibility based on selected inclusion and exclusion criteria.

Data extraction

The data were independently extracted from studies in the form as variables, according to the aims and themes of present review.

Data items

Data were collected from selected articles and arranged in the following fields:
- „Year" - describes the date of publication.
- „Type of study" - indicates the type of study.
- „Socket preservation technique" - described what biomaterial was used for socket preservation
- „Sample size" - described the number of participants in the trials.
- „Follow-up" - described the observation period.
- „Radiologic alveolar bone changes" - described the changes of alveolar ridge's width and height.
- „Histologic analysis" - described the quality of a newly formed bone regarding residual graft particles and newly formed bone ratio.

Quality assessment

Assessment of methodological study quality was performed by using criteria suggested in Cochrane Handbook for Systematic Reviews of Interventions (Higgins and Green [21]). The selected criteria were random sequence generation, allocation concealment, defined inclusion/exclusion blinding of participants and/or personnel, blinding of outcome assessment, incomplete outcome data, selective reporting. Lack of information about blinding or allocation concealments

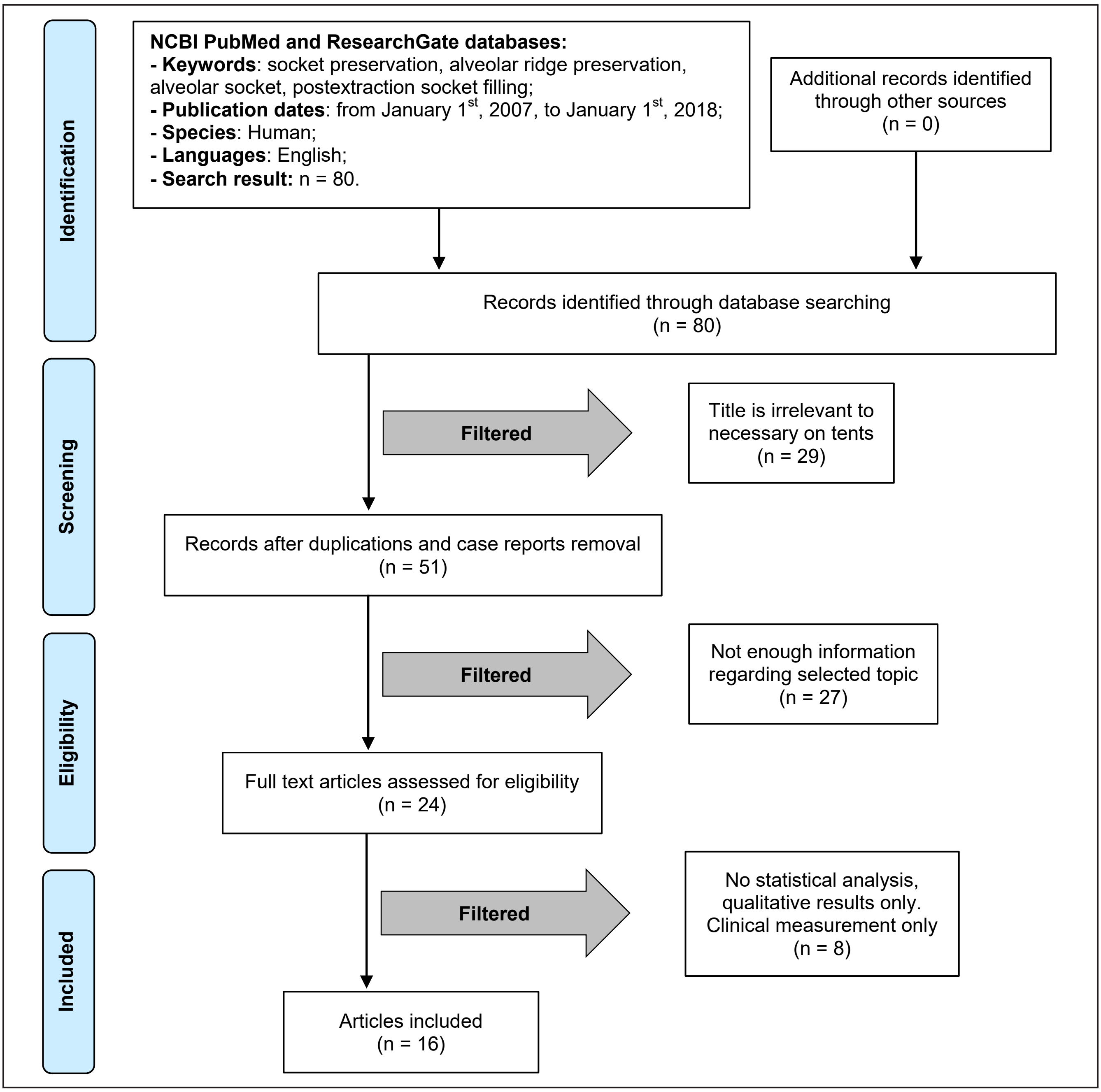

Figure 1. PRISMA flow diagram.

were not treated as relative because it could not have any impact for the study.

Synthesis of results

Appropriate data of interest on the previously stated variables were tabulated and discussed.

Statistical analysis

Heterogeneity between studies was found therefore meta-analysis could not be performed. Parametric data were expressed as mean and standard deviation (M [SD]).

Statistical significance level was defined at $P \leq 0.05$.

RESULTS

Study selection

Article review and data extraction were performed according to the PRISMA flow diagram (Figure 1). An electronic literature search was performed on the MEDLINE and Embase databases. A total of 82 search results were filtered. After inclusion of authors and exclusion criteria were applied, a number of 24 articles were selected. Finally, 16 full text articles were included in this study. List of journals included in the study is presented in Table 2.

Study exclusion

Reasons for exclusion of the study after review were: being a cases studies and no biomaterials used for socket preservation (n = 3) [22-24], insufficient amount of information regarding selected topic (n = 5) [25-29]. List of excluded studies with reasons for exclusion are presented in Table 3.

Quality assessment

Summarizing the risk of bias of each study, 16 studies were classified as low risk and no studies were ranked as high risk studies (Table 4).

Study characteristics

Finally 16 articles were included in systemic literature review. The summarized included studies characteristics are presented in Table 5.

Table 2. List of authors and full names of journal titles included in the study

Study	Journal
Thakkar et al. [30]	Contemporary Clinical Dentistry
Baniasadi and Evrard [31]	The Open Dentistry journal
Das et al. [32]	European Journal of Dentistry
Hauser et al. [33]	Implant Dentistry
Wood and Mealey [34]	Journal of Periodontology
Gholami et al. [35]	Clinical Oral Implants Research
Barone et al. [36]	The International Journal of Periodontics and Restorative Dentistry
Kotsakis et al. [37]	The International Journal of Oral & Maxillofacial Implants
Mahesh et al. [38]	Journal of Oral Implantology
Barone et al. [39]	Clinical Oral Implants Research
Canullo et al. [40]	Clinical Implant Dentistry and Related Research
Mayer et al. [41]	Clinical Implant Dentistry and Related Research
Joshi et al. [42]	Journal of Indian Society of Periodontology
Pang et al. [43]	Journal of Craniofacial Surgery
Natto et al [44]	Journal of Clinical Periodontology
Nam et al. [45]	Journal of Periodontology

Table 3. List of excluded studies with reasons for exclusion

Study	Reason for exclusion
El-Chaar [22]	Case series
Brkovic et al. [23]	Case report
Valdec et al. [24]	Case series
Carmagnola et al. [25]	No evaluation of dimensional ridge changes. Histological data regarding bone quality is not sufficient.
Milani et al. [26]	No evaluation of dimensional or histological socket changes.
Crespi et al. [27]	Only soft tissue and no biomaterials were used for socket preservation
Mozzati et al. [28]	No evaluation of dimensional ridge changes. Histological data regarding bone quality is not sufficient.
Laurito et al. [29]	No evaluation of dimensional ridge changes. Histological data regarding bone quality is not sufficient.

Table 4. Assessment of the risk of bias

Study	Year of publication	Random sequence generation	Allocation concealment	Defined inclusion/ exclusion	Blinding of participants and/or personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting
Thakkar et al. [30]	2016	N/A	N/A	+	+	+	+	+
Baniasadi and Evrard [31]	2017	N/A	N/A	-	+	+	+	+
Das et al. [32]	2016	+	N/A	+	+	+	+	+
Hauser et al. [33]	2013	+	N/A	+	+	+	+	+
Wood and Mealey [34]	2012	N/A	N/A	+	+	+	+	+
Gholami et al. [35]	2012	+	N/A	+	+	+	+	+
Barone et al. [36]	2013	N/A	N/A	+	+	+	+	+
Kotsakis et al. [37]	2014	+	N/A	+	+	+	+	+
Mahesh et al. [38]	2015	+	N/A	+	+	+	+	+
Barone et al. [39]	2013	+	N/A	+	+	+	+	+
Canullo et al. [40]	2015	N/A	N/A	+	+	+	+	+
Mayer et al. [41]	2016	+	N/A	+	+	+	+	+
Joshi et al. [42]	2016	+	N/A	+	+	+	+	+
Pang et al. [43]	2014	N/A	N/A	+	+	+	+	+
Natto et al [44]	2017	+	+	+	+	+	+	+
Nam et al. [45]	2011	N/A	N/A	+	+	+	+	+

+ = low risk; N/A = unclear risk; - = high risk.

Table 5. Comparison of bone graft materials used in the studies in terms of vertical resorption (VR), horizontal resorption (HR), residual graft particles (RG), newly formed bone (NFB) and observation period (OP)

Subgroup/study	Bio material	VR (mm)	HR (mm)	RG (%)	NFB (%)	OP (months)
Autogenous materials						
Das et al. [32]	PRF	-1.55	NM	NM	NM	6
Hauser et al. [33]	PRF	-0.98	NM	NM	NM	2
Joshi et al. [42]	Autogenous tooth graft	-0.28	-0.15	NM	NM	4
Allogenic materials						
Thakkar et al. [30]	DFDBA	-1.38	-1.36	NM	NM	6
Wood and Mealey [34]	FDBA	NM	NM	25.42	24.63	5
	DFDBA	NM	NM	8.88	38.42	5
Xenogenic materials						
Gholami et al. [35]	Bio-Oss®	-1.07	NM	20.62	27.35	7.5
Barone et al. [36]	Endobon	NM	NM	NM	28.5	6
	Bio-Oss®	NM	NM	NM	31.4	6
Kotsakis et al. [37]	Anorganic bovine bone mineral	-0.88	-1.39	NM	NM	5
Mahesh et al. [38]	Bio-Oss®	NM	NM	25.60	22.2	5
Synthetic materials						
Das et al. [32]	β-TCP	-0.99	NM	NM	NM	6
Gholami et al. [35]	NCHA	-0.93	-	13.68	28.63	7.5
Kotsakis et al. [37]	Calcium phosphosilicate	-0.83	-1.26	NM	NM	5
Mahesh et al. [38]	NovaBone®	NM	NM	17.40	47.15	5
Canullo et al. [40]	Mg-e HA	NM	NM	40.82	31.85	4
	Mg-e HA	NM	NM	26.28	41.32	12
Joshi et al. [42]	β-TCP	-1.72	-1.45	NM	NM	4
Mixed materials						
Thakkar et al. [30]	PRF + DFDBA	-1.08	-0.75	NM	NM	6
Baniasadi and Evrard [31]	PRF + DFDBA	-0.72	NM	NM	NM	3
Mayer et al. [41]	Biphasic calcium sulphate + β-TCP + HA	NM	0.03	15.99	NM	4
Pang et al. [43]	Bio-Oss® + Bio-Gide®	-1.54	-1.84	NM	NM	6
Natto et al. [44]	FDBA + CMS	-0.30	-1.21	NM	NM	4
	FDBA + CS	-0.79	-1.47	NM	NM	4
Nam et al. [45]	DBM + synthetic olygopeptide	NM	NM	NM	10.4	6

PRF = platelet rich fibrin; DFDBA = demineralized freeze-dried bone allograft; FDBA = freeze-dried bone allograft; TCP = tricalcium phosphate; HA = hydroxyapatite; DBM = demineralised bone matrix; NM = not mentioned.

Included studies were summarized according biomaterial/method used for extraction socket preservation. The studies were compared regarding vertical resorption, horizontal ridge resorption, remain of residual bone graft particles, newly formed bone and observation period. Also details of extractions (socket location, reasons for extraction, confounding factors, surgical management) performed in the studies are presented in Table 6.

Platelet concentrates

After applying exclusion criteria, 4 articles were found regarding the use of autologous platelet concentrates for alveolar socket preservation [30-33] (Table 5). There were two studies [30,31] where PRF was used in combination with demineralized freeze-dried bone allograft (DFDBA). A study by Thakkar et al. [30] showed that in a period of 6 months the reduction value of alveolar ridge width and height of PRF + DFDBA group was -0.75 (0.493) mm and -1.083 (0.429) mm respectively, and the reduction value of alveolar ridge of DFDBA alone was -1.361 (0.703) mm, -1.389 (0.502) mm. Despite the fact that the addition of PRF proved to reduce bone loss, no statistically significant difference (P = 0.056) compared to control group was found. Another study by Baniasadi and Evrard [31], had no control group and also used combination of PRF + DFDBA, showed that height reduction of alveolar bone is equal to 0.72 (0.71) mm after 3 months.

Table 6. Details of extractions

Study	Socket location	Reason for extraction	Confounding factors	Surgical management
Thakkar et al. [30]	Single-rooted teeth in maxillary and mandibular arches	Severe dental decay	None	Flapless, atraumatic extraction, wound sutured with criss-cross horizontal mattress technique
Baniasadi and Evrard [31]	Single-rooted and multi-rooted teeth in maxillary and mandibular arches	Severe dental decay, fracture, periodontal disease	30% of patients were smokers	Flapless. atraumatic extraction, wound sutured
Das et al. [32]	Isolated alveolar sockets (a socket located between two sound teeth) of maxillary and mandibular single-rooted teeth	Caries, endodontic complications (e.g., root fracture), periodontitis, and prosthetic reason	None	Muco-periosteal envelope flap, atraumatic extraction, cross-mattress sutures to close the wound
Hauser et al. [33]	Premolars of maxillary and mandibular arches	Endodontic treatment failures, root fractures, advanced caries lesions, and periodontally compromised teeth	Not available	A buccal and palatal/lingual mucosal flap, wound sutured with a point-cross technique
Wood and Mealey [34]	Single-rooted teeth in maxillary and mandibular arches	Not available	None	Flapless, atraumatic extraction, wound sutured
Gholami et al. [35]	Non-molar teeth in maxillary and mandibular arches	Endodontic treatment failures, trauma, prosthetic issues	None	Buccal mucosal flap, atraumatic extraction, flap sutured to allow tension-free primary closure
Barone et al. [36]	Premolars and molars in maxillary and mandibular arches	Severe decay, failed endodontic treatment, periodontal disease, fractures	None	Flapless, atraumatic extraction, socket covered with collagen membrane, wound sutured without marginal closure
Kotsakis et al. [37]	Not available	Not available	Smoking (< 10 cigarettes a day)	Flapless, atraumatic extraction, wound closed with a horizontal mattress suture
Mahesh et al. [38]	Single-rooted teeth in maxillary and mandibular arches	Not available	Smoking (< 10 cigarettes a day)	Flapless extraction, wound sutured using horizontal mattress suture
Barone et al. [39]	Not available	Not available	Smoking (< 10 cigarettes a day)	Flapless, atraumatic extraction, wound covered with collagen membrane and sutured
Canullo et al. [40]	Maxillary premolars	Not available	None	Flapless, atraumatic extraction, wound covered with collagen membrane
Mayer et al. [41]	Not available	Not available	Smoking (< 10 cigarettes a day)	Muco-periosteal flap, atraumatic extraction, wound sutured and primary closure ensured
Joshi et al. [42]	Not available	Not available	Not available	Flapless, atraumatic extraction, socket covered with collagen membrane, one criss-cross suture to stabilize the membrane
Pang et al. [43]	Not available	Not available	None	Rectangular full-thickness flap, atraumatic extraction, socket covered with collagene membrane, wound sutured
Natto et al [44]	Single-rooted tooth (excluding lower incisors)	Caries, endodontic complication, root fracture, or trauma with no evidence of acute infection	Smoking (< 10 cigarettes a day)	Flapless, atraumatic extraction, socket covered with collagen membrane, wound closed with horizontal mattress suture
Nam et al. [45]	Not available	Advanced periodontal and/or endodontic lesion	Not available	A buccal and palatal/lingual mucosal flap, atraumatic extraction, flaps sutured using interrupted and vertical mattress sutures

Results of PRF application alone [32,33] demonstrated that platelet concentrates help to reduce resorption of alveolar ridge. In a clinic-radiographic study [32] where socket filling with PRF was compared to β-tri-calcium phosphate (β-TCP), the results showed that 6 months after extraction alveolar ridge resorption reached -1.55 mm in sockets filled with PRF. It had a statistically significant difference ($P = 0.001$) in comparison to resorption in sockets filled with β-TCP (-0.99 mm). Findings of this study show that β-TCP is more effective in preventing height loss of alveolar ridge. Despite that, histological findings of this same study demonstrate that sockets filled with PRF have well-formed bony trabeculae with adequate medullary spaces, filled with fatty tissue, whereas biopsies of sockets filled with β-TCP show evident foci of amorphous eosinophilic deposits, possibly remnants of graft material. This indicates that PRF helps to form bone of a better quality. In another study with an observation period of eight weeks [33] PRF also proved to be a successful socket preservation method as the height of alveolar ridge decreased only by 0.985 mm in PRF group. It was significantly less ($P < 0.05$) compared to natural clot group where mean resorption was 1.42 mm. Micro-CT analysis in this same study also revealed that newly formed bone in PRF group had significantly more density (820 mmHA/ccm) than group of a natural clot (780 mmHA/ccm). This indicates that PRF not only reduces dimensional changes, but also helps to form new bone of a higher quality.

Allogenic materials

Wood and Mealey [34] compared mineralized freeze-dried bone allograft (FDBA) with DFDBA in terms of quality of a newly formed bone (Table 3). Histological analysis of determining percentage of newly formed bone, residual graft material and connective tissue showed that DFDBA had a significantly greater percentage of newly formed bone: 38.42 (14.48)% versus 24.63 (13.65)%. DFDBA also had significantly lower percentage of residual bone graft particles: 8.88 (12.83)% versus 25.42 (17.01)%. These results show that DFDBA is significantly greater in alveolar ridge preservation and new bone formation.

Xenogenic materials

Five studies [35-39] were found considering usage of xenografts for socket preservation (Table 3). In one of the studies [35] bovine xenograft (DBBM, Bio-Oss®) was used in comparison to synthetic nanocrystalline hydroxyapatite (NCHA). After a 6 - 8 month post-extraction observation period, results showed that horizontal alveolar ridge width reduction was statistically significant ($P < 0.05$) in both groups: -1.07 (0.97) mm and -0.93 (0.57) mm for DBBM and NCHA groups respectively, but no statistically significant difference was found between the groups. Histologic analysis of the study also revealed that both materials have similar effectiveness. Although values of different variables were not the same, i.e. in DBBM group: residual graft particles 20.62 (9.91) %, newly formed bone 27.35 (12.39) %, bone marrow 52.03 (14.7) %; in NCHA group: residual graft particles 13.68 (8.07) %, newly formed bone 28.63 (12.53) %, bone marrow 57.69 (11.85) %, no statistically significant differences were found.

Barone et al. [36] compared two different commercially available bovine bone xenografts: Endobon (test group) and Bio-Oss® (control group). The study aimed mostly for histologic outcomes and revealed that both materials are similar in effectiveness, when it comes to a formation of a new bone, Endobon: 28.5 (20) %, Bio-Oss® 31.4 (18) %.

A study by Kotsakis et al. [37] compared particulate anorganic bovine bone mineral (BOV) and calcium phosphosilicate putty bone substitutes (PUT) to each other and to a natural healing control group. Findings of this study show that after observation period of 5 months both BOV and PUT helped to reduce loss of alveolar ridge height when compared to natural healing, -0.88 (0.3) mm, -0.83 (0.32) mm and -1.12 (0.23) mm respectively, although no statistically significant difference was found. Horizontal changes of alveolar ridge differed significantly ($P < 0.05$) between BOV and PUT groups and compared to the control group: -1.39 (0.57) mm, -1.26 (0.41) mm and -2.56 (0.59) mm respectively.

A similar study where putty alloplastic bone substitute (CPS) was compared to particulate anorganic bovine xenograft (BO) was conducted by Mahesh et al. [38]. The study aimed to evaluate the quality of a newly formed bone and the results showed that the amount of residual graft values was significantly higher in BO group compared to CPS group, 25.6 (5.89)% and 17.4 (9.39)% respectively. The amount of newly formed bone was also in favour of CPS group where it reached 47.15 (8.5)% compared to 22.2 (3.5)% in BO group ($P < 0.05$). Findings of this study indicate that CPS is a better material for socket preservation considering quality of the bone, even though both type of materials show similar results when it comes to dimensional changes of alveolar socket as described in previously presented study [38].

Another study regarding socket preservation [39] was carried out by using corticocancellous porcine bone graft to fill sockets after extraction and comparing it to natural clot (control group). The results of this study showed that selected graft material helps to prevent bone loss after the extraction. After 4 months of observation vertical resorption reached mean of 1.1 (0.96) mm whereas horizontal width was reduced by 1.6 (0.55) mm in corticocancellous graft group which was less compared to control group where vertical and horizontal resorption reached -2.1 (0.6) mm and -3.6 (0.72) mm respectively.

Synthetic materials

Another study by Canullo et al. [40] concerning magnesium-enriched hydroxyapatite (Mg-e HA) histologically and histomorphometrically analysed extraction sockets filled with Mg-e HA. Four and 12 months after socket preservation, bone sample was harvested and histological analysis was processed considering newly formed bone, residual bone substitute and medullary spaces ratio. 4-month histomorphometric analysis showed: 31.85 (6.99)% newly formed bone; 40.82 (6.71)% residual biomaterial; 27.3 (7.72)% medullary spaces. Twelve months after socket preservation, the results were: 41.32 (9.37)% bone; 26.28 (11.49)% residual biomaterial; 32.4 (9.87)% medullary spaces. The study showed that Mg-e HA allows a complete healing of extraction socket.

A comparison between composite materials (biphasic calcium sulphate (BCS) with β-TCP and HA, test group) and natural socket healing (control group) indicated that these materials can be used as a method for socket preservation [41]. Results of the study showed that after 4 months horizontal width changes differed statistically ($P = 0.007$) between test and control groups. While the width in test group increased by 0.03 (2.32) mm, control group lost 2.28 (2.36) mm of horizontal width. Histologic analysis revealed that both groups presented with vital new bone formations with no inflammatory response and only the amount of connective tissue had statistically significant difference ($P = 0.013$), test group: 36.3 (19.4)%, control group: 46.7 (10.6)%.

In the experimental study carried out by Joshi et al. [42] β-TCP was used for socket preservation and then compared to autogenous tooth graft (ATG). 4 months after the tooth extraction vertical bone loss in ATG group was 0.28 (0.13) mm which was significantly lower ($P < 0.05$) compared to β-TCP-grafted sites where resorption reached 1.72 (0.56) mm reduction and ungrafted sites with 2.6 (0.88) mm reduction. Considering horizontal width changes in ATG, which with the resorption of 0.15 (0.18) mm, was significantly ($P < 0.05$) more efficient compared to β-TCP grafted sites and ungrafted sites where horizontal resorption reached -1.45 (0.4) mm and -2.29 (0.4) mm respectively. Histological findings also proved ATG to be superior. Specimens from ATG-grafted sites showed newly formed bone associated with connective tissue stroma rich in angiogenesis. ATG particles had started to resorb and were surrounded by osteoid indicating new bone formation, whereas β-TCP-grafted sites presented less osteoid formation, graft particles were poorly integrated with newly forming bone with minimal evidence of angiogenesis.

Combination of several biomaterials

Pang et al. [43] compared extraction sockets filled with deproteinized bovine bone graft (Bio-Oss®, Geistlich Pharma AG, Wolhusen, Switzerland) covered with absorbable collagen membrane (Bio-Gide®, Geistlich Pharma AG, Wolhusen, Switzerland) (test group) and sockets healed without any grafting material. The goal of study was to evaluate and compare panoramic radiograph and computed tomography (CT) after different periods of time. Results showed a significant difference in alveolar width, height and volume reduction in both groups (height reduction in test group was 1.05 (0.24) mm at 3 months, 1.54 (0.25) mm at 6 months; width reduction was 1.11 (0.13) mm at 3 months and 1.84 (0.35) mm at 6 months; bone volume reduction was 193.79 (21.47) mm^3 at 3 months and 262 (33.08) mm^3 at 6 months. Height reduction in control group was 2.12 (0.15) mm at 3 months and 3.26 (0.29) at 6 months, the width reduction was 2.72 (0.19) mm at 3 months and 3.56 (0.28) mm at 6 months. Bone volume reduction - 252.19 (37.21) mm^3 at 3 months and 342.32 (36.41) mm^3 at 6 months. The results after 12 months showed that grafted socket had no difference for implant osseointegration and stability. It also says that GBR technique is suitable for alveolar ridge preservation.

Natto et al. [44] clinical study revealed that ridge preservation using either collagen matrix seal (CMS) or collagen sponge (CS) in combination with FDBA minimize alveolar ridge resorption rate in all dimensions. 4 months after extraction and socket filling with regenerative materials, reduction of alveolar ridge was: 1.21 (1.22) mm width and 0.3 (1.09) mm vertical reduction in CMS, whereas CS presented 1.47 (1.29) mm width and 0.79 (3.07) mm vertical resorption. The difference was not statistically significant.

Comparison of deproteinized-bovine-bone mineral coated with synthetic oligopeptide (test group) with extraction socket healed spontaneously showed less resorption and a higher tendency for new bone formation in the test group [45]. The percentage of new bone formation was higher in peptide-modified group: 10.4 (4.6)% versus 5.3 (8.3)%. Also it has showed that in peptide-modified group bone graft particles mostly localized in borders of bone defects while bone particles in the centre of the defect were surrounded by new bone.

DISCUSSION

The main goal of this systematic review was to evaluate materials and methods used to maintain alveolar ridge height, width and bone quality. Most studies which investigated soft and hard tissue dimensional changes after tooth extraction states that ideal bone graft material should not only have osteoconductive properties but also promote osteoinduction and osteogenesis [46,47]. Only autologous bone has these three properties and is still considered to be the gold standard for bone augmentation procedures. Nevertheless, extra site of operation and prolonged time of surgery, donor side morbidity, limited autologous bone availability and postoperative discomfort leads to the use of alternative bone substitutes for bone regeneration. Bone graft materials are chosen based on their ability to serve as a scaffold, maintain space for new bone ingrowth and possess only osteoconductive activity [48]. Only DFDBA has osteoinductive properties. It serves not only as a scaffold for new bone regeneration but also stimulates the differentiation of mesenchymal cells into osteoblasts [49]. Many studies that investigated DFDBA state that demineralization of allogenic bone results in exposure of inner structure of bone graft, which contains bone morphogenetic proteins and growth factors that have osteoinductive potential [49-55].

Tooth extraction results in bundle bone loss, which causes alveolar ridge resorption. As a consequence of alveolar bone resorption, soft tissue shrinkage occurs. Even the most conservative tooth extraction can cause bone resorption and lead to the necessity of bone augmentation procedure during implant placement, especially in aesthetic area. More bone loss in expense of buccal cortical plate occurs for patients with thin periodontal type [56]. In presence of marginal bone pathology or traumatic extraction when there is an absence of bony wall fibrous tissue will ingrowth in a part of extraction socket and interfere normal healing and bone regeneration [57]. Alveolar ridge preservation after tooth extraction can eliminate the need of bone augmentation procedure during implant placement. It also reduces the risk of complications and cost of the treatment [58]. However, sufficient alveolar ridge dimensions for implant placement is important, it is also necessary that the regenerated bone is of good quality. It was stated that the quality and quantity of regenerated bone influence the primary stability of implant and can determine the success of dental implant osseointegration [59-61]. Many studies emphasize the correlation between bone quality and primary implant stability which determines success of implantation [59,60,62,63]. Therefore, considering extraction socket preservation, it is important to reduce bone resorption and to regenerate high quality bone.

There are many different alveolar ridge preservation techniques after tooth extraction. The main goal of the bone graft material is to serve as a scaffold and maintain a space for bone ingrowth, blood vessels formation, to support soft tissues and to improve the quality and quantity of regenerated bone [64].

This systematic review analysed evidence based alveolar ridge preservation techniques and states that complete prevention of vertical resorption is still not implemented. Only one preservation technique in Mayer et al. [41] not only stopped horizontal resorption, but actually increased width of alveolar ridge. Considering our focus questions, biomaterials which helped to reduce vertical resorption the most during different observation periods was autogenous tooth graft: -0.28 (0.13) mm, observation period (OP): 4 months, [42] and NCHA (nanocrystalline hydroxyapatite): -0.93 (0.57) mm, OP: > 6 months [34]. The least effective techniques on this matter, not including natural healing because in all cases this group showed worse results than selected preservation technique, were β-TCP: -1.72 (0.56) mm, OP: 4 months [34], and PRF: -1.55mm, OP: 6 months [32]. When it comes to horizontal resorption, the most effective techniques were biphasic calcium sulphate + β-TCP + HA: 0.03 (2.32) mm, OP: 4 months [41], and calcium phosphosilicate: -1.26 (0.41) mm, OP: 6 months [37], while the worst results, not including natural clot groups, were presented when using β-TCP: -1.45 (0.4) mm, OP: 4 months [42], and Bio-Oss® + Bio-Gide® membrane: -1.84 (0.35) mm, OP: 6 months [43]. Comparing the quality of newly formed bone, the best results, considering residual graft particles and newly formed bone ratio, are achieved when using DFDBA: RG: 8.88 (12.83)%, NFB: 38.42 (14.48)%, OP: 5 months [34], and the least effective biomaterial on that matter seems to be the combination of Mg + HA: RG: 40.82 (6.71)%, NFB: 31.85 (6.99)%, OP: 4 months [40].

Despite the fact that platelet rich concentrates demonstrated high vertical resorption rate (-1.55mm, OP: 6 months) [24], histological findings show that it stimulated new bone formation of higher quality. Micro-CT analysis of platelet rich concentrates in comparison with natural clot revealed significantly denser bone in platelet rich concentrates group (820 mmHA/ccm vs. 780 mmHA/ccm) [32]. Platelet concentrates seem to not only help a formation of better quality bone but also improve qualities of other biomaterials when combined together which results in a smaller dimensional changes. These findings agree with the results reported in other reviews in which autologous platelet concentrates proved to be beneficial for both quantity [65] and quality of a newly formed bone [66,67].

This systematic review revealed that currently there are insufficient clinical evidence to state which extraction socket preservation method would be optimal to reduce bone resorption and to improve bone quality of regenerated bone. In addition to that, there was a lack of indications when to perform extraction socket preservation. In cases of thick periodontal biotype in non-aesthetic area with no demand for vertical bone dimension, spontaneous healing or platelet rich concentrates are suggested. Furthermore, it is impossible to determine which method for alveolar ridge preservation is better because preservation techniques were analysed in different localization of jaws and the studies compared different evaluation/investigation methods. To avoid additional bone augmentation procedures, soft tissue recessions to maintain enough alveolar bone for successful implant placement alveolar ridge preservation is suggested. Considering correlation between the bone quality and quantity future studies of combining platelet rich concentrates and bone graft materials are needed.

CONCLUSIONS

The systematic review of extraction socket preservation using different techniques and biomaterials revealed that there is no "gold standard" to preserve alveolar ridge and none of the found techniques managed to completely stop alveolar resorption. Considering different alveolar socket preservation techniques it is impossible to evaluate objectively which biomaterial and method is better because studies were performed in different areas of jaws, different observation methods and periods were used. The majority of studies state that alveolar socket preservation decreases vertical and horizontal alveolar bone resorption, shows better preservation of keratinized tissue. Considering alveolar ridge resorption and quality of newly formed bone, the best results were achieved using demineralized freeze-dried bone allograft. The use of autologous platelet concentrates was effective in socket preservation and results considering bone resorption were similar to bone graft materials, therefore being autologous, accelerating healing and soft tissue epithelialization while also reducing postoperative pain. Regenerative material, platelet concentrates are suggested to be used in cases when bone graft material is not strictly beneficial for clinical use. Considering correlation between bone quality and quantity future studies of combining platelet rich concentrates and bone graft materials are needed.

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The authors report no conflicts of interest related to this study.

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