Journal of Craniomaxillofacial Research

Vol. 12, Issue. 3 Summer 2025

Efficacy of SocketKAGE™ and SocketKAP™: A Review

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ARTICLE INFO

Article Type:
Review Article

Received: 12 April 2024
Revised: 12 May 2024
Accepted: 19 July 2025

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ABSTRACT

Introduction: This study aims to determine whether the application of SocketKAP™ (KAP) and SocketKAGE™ (KAGE) in tooth extraction sockets can reduce alveolar ridge changes.

Materials and Methods: An electronic search of PubMed, Google Scholar, Scopus and Web of Science databases was conducted up to September 2024. Screening and data extraction were performed independently by two researchers. Three randomized clinical trials (RCTs) were included. This systematic review was done according to the PRISMA 2020 guideline.

Results: All studies showed that KAP alone and KAP+Anorganic bovine bone mineral (ABBM) significantly decreased contour loss in human intact sockets compared with no intervention. KAP+ABBM significantly decreased alveolar bone volume loss in human intact sockets compared with no intervention. KAGE+KAP+ABBM significantly decreased contour loss and alveolar bone volume loss in human sockets with dehiscence compared with no intervention.

Conclusion: The review suggests that KAP and KAGE may be beneficial in reducing alveolar ridge changes, but it is recommended that further studies be conducted to confirm the findings of the review and to determine whether KAP and KAGE are cost-effective interventions for reducing alveolar ridge changes.

Keywords: Alveolar bone grafting; Alveolar process; Bonesubstitute; Tooth extraction; Tooth socket; Wound healing; KAGE™; KAP™.

Please cite this Article as:
Salmani Z, Abedini F, Chokami Rafiei S. Efficacy of SocketKAGE™ and SocketKAP™: A Review. J Craniomaxillofac Res 2025; 12(3): 134-147. DOI: 10.18502/jcr.v12i3.20621

Introduction

Alveolar ridge resorption after tooth extraction is a common complication that complicates implant placement [1]. Ridge preservation refers to the application of different materials and techniques to minimize alveolar ridge changes after tooth extraction [2-5] and decrease the need for ridge augmentation surgical procedures for implant placement [6-8]. Atraumatic tooth extraction, immediate implant placement in the extraction socket, covering the socket opening with a membrane, and socket grafting with biomaterials and biologically active materials are among the suggested techniques for socket preservation [5,9-12]. Graft materials serve as a mechanical support for the membrane during the healing phase, and play a role as a stimulant or scaffold for bone regeneration [13-15]. Allografts do not require a second surgical site and, therefore, are associated with decreased host morbidity. Also, they are easily available in abundance and therefore, are extensively used for regeneration therapy and ridge preservation [16,17].

Too small allograft particles (< 125 μm) cause macrophage reaction without new bone regeneration. Also, small particles may remain at the site for a couple of months to years [17]. Xenografts are mostly osteoconductive and less osteoinductive. Histological findings indicate optimal homogeneity and blending of bovine xenograft particles with the newly formed bone [16]. Evidence shows that Bio-Oss, which is used as a bone remodeling scaffold, does not induce new bone formation [17]. Alloplasts are a group of synthetic osteoconductive and biological filler materials. The commonly used alloplasts include hydroxyapatite, tricalcium phosphate, calcium sulfate, and bioactive glass polymers. Risk of infection or disease transmission does not exist in use of alloplasts and they can be used indefinitely [16-18]. However, when used for regeneration of bone defects, they have limited periodontal regenerative capacity [18]. Autogenous bone is a biocompatible material with the potential to induce new bone formation. Autogenous bone has osteogenic, osteoconductive, and osteoinductive properties [13]. However, its limited availability, donor site morbidity, unpredictable bone quality, and postoperative discomfort are among the drawbacks of autogenous bone [8]. Araujo and Lindhe found that autogenous graft was unsuccessful in new bone formation and prevention of ridge resorption after tooth extraction compared with xenografts [3]. Nonabsorbable membranes such as titanium and expanded polytetrafluoroethylene (ePTFE) have long been successfully used for guided bone regeneration [19,20]. They preserve adequate space for stable bone regeneration and do not adhere to the tissue. Thus, they can be easily removed without traumatization of the underlying tissue after elevating a flap [21]. One problem of nonabsorbable membranes is their three-dimensional positioning at the socket opening [5]. Exposure of these membranes increases the risk of infection and negatively affects the process of tissue regeneration. Absorbable membranes have advantages such as being absorbable and simple surgical technique. They are highly biocompatible and flexible, and have low risk of early exposure [3,17]. However, their application is questionable since they delay the process of healing as they have variable resorption rates and require a tenting screw. They also have the risk of displacement [3].

Zadeh et al., in 2016, were the first to assess the efficacy of SocketKAP™ (KAP) and SocketKAGE™ (KAGE) for ridge preservation. KAP is a dome-shaped non-resorbable device available in different sizes, which is made of polypropylene and has holes in its external part for suturing. It can be used in both intact and dehiscence sockets [12]. KAGE is an absorbable instrument with inter-connected ribs made of poly-L/D-lactide (PLLA) [2,12] that preserves the facial dehiscence defect space [2,6,8]. KAGE supports and preserves the three-dimensional contour of the alveolar ridge and prevents tissue collapse during the healing phase. It is used not only for preservation, but also for reconstruction of alveolar ridge defects [2,5]. The main goal of this review is to answer the question of whether the application of SocketKAP™ and SocketKAGE™ in tooth extraction sockets can decrease alveolar ridge changes or not.

Materials and Methods

This systematic review was done according to the PRISMA guideline [22]. To assess the efficacy of SocketKAGETM and SocketKAPTM for Alveolar Ridge Preservation. We conducted a systematic review of all related studies, which were searched from comprehensive international databases up to March 202.

Information sources and literature search strategy

An electronic search was performed in Scopus, Web of Science, PubMed, and Google Scholar databases. Keywords used in electronic database search included ("alveolar ridge preservation" OR "ridge preservation" OR "socket graft" OR "socket grafting" OR "extraction socket" OR "socket preservation" OR "socket augmentation" OR "socket management") AND ("Socket-

KAP“ OR “SocketKAGE “ OR Socket KAP OR Socket KAGE). This process was repeated until no new study was found. The final electronic search was conducted in September 2024. The titles and the abstracts of the retrieved articles were evaluated by two independent reviewers (S.C.R. and Z.S.).

Inclusion/exclusion criteria

The eligible studies were chosen based on inclusion/exclusion criteria that were determined a priori according to the participant-intervention-comparison-outcome-study (PICOS) schema:

- Population: Tooth extraction sockets that require grafting.
- Intervention: Use of KAP and KAGE in tooth extraction sockets.
- Comparison: Comparison of KAP, KAGE and KAP+KAGE or their combination with biomaterial fillers with a control group.
- Outcome: Alveolar ridge changes after tooth extraction.

Study design: All studies with a minimum follow-up period of 3 months that used KAP and KAGE for socket preservation and were published until September 2024 were included.

The following exclusion criteria were applied: **(1)** duplicate publication and **(2)** recruitment of patients with certain specific systemic diseases. **(3)** non-research article, including letter to editor, abstract. **(4)** Items that did not have a good quality assessment.

Study selection

The resulting studies after applying inclusion/exclusion criteria were first checked for duplicates, then the titles and abstracts were screened for relevance. The final stage involved retrieving and checking the full texts. The process was conducted independently by two of the authors (S.C.R. and Z.S.), and any conflicts were resolved by consulting a third author (F.A.).

Quality assessment of human studies

The Cochrane Alliance tool was utilized to recognize potential risk of bias for the randomized controlled trials [23]. The risk of bias within each study was classified as follows: low risk of bias if all criteria were encountered, debatable risk of bias if 1 criterion was missing, and high risk of bias if no fewer than 2 criteria were missing.

Quality assessment of animal studies

A quality assessment of all selected full-text animal articles was performed according to the ARRIVE guidelines for reporting in vivo experiments in animal research [23]. This guideline contains a checklist of 20 items and is prepared using the CONSORT command as its basis (Table 1).

Results

The search yielded 71 articles (A total of 55 articles were retrieved from Google Scholar, 6 articles were retrieved from PubMed, 5 articles were retrieved from Scopus, and 5 articles were retrieved from the Web of Science following database searching). Three full texts (3 RCTs) and 4 animal studies) were retrieved from these initial results, after eliminating duplicates and checking titles and abstracts. The flow diagram of the systematic review is presented in Figure 1. One study assessed the alveolar ridge contour including soft tissue changes [12], 2 studies evaluated the changes in alveolar ridge volume [5,6], one studies assessed the linear changes of alveolar ridge [24], and 3 studies evaluated histological parameters [2,8,25]. The follow-up period ranged from 3 months to 6 months (Table 2).

Risk of Bias Assessment

All of the three-included randomized controlled trials were identified with a high risk of bias (Table 3). Quality assessment of included animal studies in different categories per checklist item are summarized in Table 4. In particular, all of the included animal studies were associated with minimum Grading when evaluating checklist items 4 (Introduction/Primary and secondary objectives), 9 (Methods/Housing and husbandry), 10 (i.e., Methods/Sample size), 14 (Results/Baseline data), and 17 (Results/Adverse events). For item 19 (i.e., Discussion/Generalisability), all of the included animal studies were graded with medium scores. For checklist item 8 (i.e., Methods/Experimental animals), medium grading was assigned to Kyung-Ho Ryu et al.'s study. For other checklist items, maximum gradings were assigned to the included publications.

Assessment of changes in alveolar ridge contour

Zadeh et al.reported that 6 months after tooth extraction, treatment with KAP alone and KAP+anorganic bovine bone mineral (ABBM) significantly decreased contour loss in intact sockets at 0-3mm apical to the alveolar crest compared with the control sockets that received no intervention. Comparison of KAP+ABBM versus KAP alone showed a significant

DOI: 10.18502/jcr.v12i3.20621

difference in favor of treatment with KAP+ABBM at 6-9mm apical to the alveolar crest in intact sockets. Application of KAGE+KAP+ABBM significantly decreased contour loss at 0-3 mm apical to the alveolar crest of sockets with buccal dehiscence compared with control sockets that received no intervention [26].

Assessment of changes in alveolar ridge volume

Abdelhamid A et al.reported that 6 months after tooth extraction, treatment with KAP+ABBM significantly decreased alveolar bone volume loss at 0-3 mm apical to the alveolar crest in intact sockets, compared with control sockets that received no intervention [27]. The difference in the percentage of alveolar bone volume loss in the sockets treated with KAP+ABBM was not significant in any part compared with sockets treated with KAP alone. However, treatment with KAGE+KAP+ABBM significantly decreased alveolar bone volume loss at 0-3 mm apical to the alveolar crest in sockets with buccal dehiscence compared with the control sockets. An animal study 4 reported that application of KAP+ABBM significantly decreased alveolar bone volume loss at 0-3 mm, and 3-6 mm apical to the alveolar crest in intact sockets compared with the control sockets at 6 and 12 weeks after tooth extraction.

Application of KAP alone in intact sockets significantly decreased alveolar bone volume loss at 3-6 mm apical to the alveolar crest, compared with the control sockets. An interesting finding was that no treatment or treatment with KAP+ABBM caused new bone formation at 6-9 mm apical to the alveolar crest in intact sockets after 6 and 12 weeks. In sockets with buccal dehiscence, treatment with KAGE+ABBM or KAGE+KAP+ABBM significantly decreased alveolar bone volume loss at 0-3 mm and 3-6 mm apical to the alveolar crest at 6 weeks after tooth extraction, and at 0-3 mm apical to the alveolar crest at 12 weeks after tooth extraction, compared with the control sockets. The alveolar bone volume loss at 0-3 mm apical to the alveolar crest at 6 and 12 weeks post-extraction was significantly lower in sockets treated with KAGE+KAP+ABBM compared with those treated with KAGE+ABBM. At 6-9 mm apical to the alveolar crest, treatment with KAGE+KAP+ABBM caused new bone formation at 6 (bone gain: 2.3%) and 12 (bone gain: 5.7%) weeks.

Assessment of linear changes of alveolar ridge

In sockets with dehiscence, application of KAGE+KAP+ABBM significantly decreased width loss at 2 mm apical to the crest compared with treatment with KAGE+KAP and no treatment. Application of KAGE +KAP+ABBM significantly decreased bone surface loss compared with treatment with KAGE+KAP and no treatment. Application of KAGE+KAP+ABBM and KAGE+KAP significantly decreased the loss of bone height at 2mm apical to the crest in sockets with buccal dehiscence compared with no treatment. Another animal study 25 reported that application of KAP+ABBM in intact sockets significantly decreased bone width loss at 1 and 2 mm apical to the alveolar crest at 6 weeks compared with no treatment, and treatment with KAP alone. Application of KAP+ABBM in intact sockets significantly decreased bone width loss after 12 weeks compared with no treatment at 1, 2, and 3 mm apical to the crest, and compared with treatment with KAP at 1 and 2 mm apical to the crest. Treatment with KAP+ABBM significantly decreased bone height loss in the buccal third of intact sockets after 6 weeks, compared with no treatment. At 12 weeks after tooth extraction, treatment with KAP alone and KAP+ABBM significantly decreased bone height loss in the buccal third of intact sockets compared with no treatment.

In sockets with dehiscence, KAGE+KAP+ABBM significantly decreased bone width loss at 3mm apical to the crest after 6 weeks, compared with no treatment and treatment with KAGE+KAP, and at 2 and 5 mm apical to the crest compared with no treatment. Treatment with KAGE+KAP significantly decreased bone width loss in sockets with dehiscence after 6 weeks at 1, 2, and 3 mm apical to the crest, compared with no treatment. Treatment with KAGE+KAP+ABBM after 12 weeks significantly decreased bone width loss in sockets with dehiscence at 2 and 3 mm apical to the crest compared with no treatment, and treatment with KAGE+KAP, and at 5 mm apical to the crest compared with treatment with KAGE+KAP. Treatment with KAGE+KAP+ABBM after 6 weeks significantly decreased bone height loss in the buccal third of sockets with dehiscence compared with no treatment, and in the middle third compared with KAGE+KAP. Treatment with KAGE+KAP+ABBM after 12 weeks significantly decreased bone height loss in sockets with dehiscence compared with treatment with KAGE+KAP in the buccal third.

Histological and histomorphometric assessments

Ryu KH et al.showed that no treatment resulted in a significant collapse of crestal bone and the overlying soft tissue. Treatment with KAP alone resulted in the formation of a relatively smooth crestal ridge contour and moderate soft tissue collapse. Treatment with

KAP+ABBM resulted in a convex crestal ridge contour, which had a slightly more coronal position than the adjacent parts of the ridge. At 12 weeks after tooth extraction, no treatment, and treatment with KAP alone with no bone grafting resulted in higher amounts of mature lamellar bone compared with sockets treated with KAP+ABBM. Application of KAP+ABBM resulted in the formation of less mature woven bone and moderate amounts of residual ABBM particles. The percentage of viable bone following the application of KAP alone and KAP+ABBM was higher than that in untreated sockets. At 12 weeks, no significant difference was noted in the amount of viable bone between treatment with KAP alone and KAP+ABBM [28]. The results of an RCT showed that at 6 months after tooth extraction, treatment without application of any biomaterial resulted in higher percentage of viable bone. In use of KAP alone, and in untreated sockets, mature organized lamellar bone, along with secondary osteons, was noted. In KAP+ABBM and KAGE+KAP+ABBM groups, mineralized tissue, bone marrow, and limited amounts of connective tissue were noted. The mineralized tissue was mainly composed of woven bone, and small amounts of lamellar bone were noted. Treatment with KAP+ABBM resulted in 33.61% residual graft particles, while treatment with KAGE+KAP+ABBM resulted in 29.05% residual graft particles. At 6 months after treatment with KAGE+KAP+ABBM, no PLLA residues were seen [2]. Another animal study reported that at 12 weeks after tooth extraction, treatment of intact sockets with KAP+ABBM (19%) decreased the percentage of viable bone compared with treatment with KAP alone (48%) and no treatment (42%). Treatment with KAP+ABBM (39%) decreased the percentage of voids compared with treatment with KAP alone (52%) or no treatment (58%). Treatment with KAP+ABBM resulted in 42% residual ABBM particles. Also, treatment with KAP+ABBM resulted in the formation of immature woven bone and lamellar bone along with reversal lines, which indicated active bone remodeling [24].

Regarding the sockets with dehiscence, treatment with KAGE+KAP+ABBM decreased the percentage of viable bone compared with treatment with KAGE+KAP and no treatment. Treatment with KAGE+KAP+ABBM decreased the percentage of voids compared with KAGE+KAP and no treatment. Treatment with KAGE+KAP+ABBM resulted in 35% residual ABBM particles. Histologically, sockets with dehiscence treated with KAGE+KAP showed PLLA residues, while those treated with KAGE+KAP and untreated sockets showed formation of lamellar bone and reversal lines.

Table 1. Categories to assess the quality of finally selected studies (Kilkenny et al. 2010a).

Item	*Description*	*Grading*
1	*TITLE*	*0 = inaccurate/not concise* *1 = accurate and concise*
2	*ABSTRACT*	*0 = clearly inaccurate* *1 = possibly accurate* *2 = clearly accurate*
3	*INTRODUCTION* *Background–objectives, experimental approach and rationale, relevance to human biology*	*0 = clearly insufficient* *1 = possibly sufficient* *2 = clearly sufficient*
4	*INTRODUCTION* *Objectives – primary and secondary*	*0 = not clear* *1 = clear*
5	*METHODS* *Ethical statement–nature of the review permission, relevant licences, national and institutional guidelines for the care and use of animals*	*0 = clearly insufficient* *1 = possibly sufficient* *2 = clearly sufficient*
6	*METHODS* *Study design–number of experimental and control groups, any steps taken to minimize bias (i.e. allocation concealment, randomisation, blinding)*	*0 = clearly insufficient* *1 = possibly sufficient* *2 = clearly sufficient*
7	*METHODS* *Experimental procedure–precise details (i.e. how, when, where, why)*	*0 = clearly insufficient* *1 = possibly sufficient* *2 = clearly sufficient*

DOI: 10.18502/jcr.v12i3.20621

Item	Description	Grading
8	METHODS Experimental animals–species, strain, sex, developmental stage, weight, source of animals	0 = clearly insufficient 1 = possibly sufficient 2 = clearly sufficient
9	METHODS Housing and husbandry – conditions and welfare-related assessments and interventions	0 = clearly insufficient 1 = possibly sufficient 2 = clearly sufficient
10	METHODS Sample size–total number of animals used in each experimental group, details of calculation	0 = clearly insufficient 1 = possibly sufficient 2 = clearly sufficient
11	METHODS Allocation animals to experimental groups–randomisation or matching, order in which animals were treated and assessed	0 = no 1 = yes
12	METHODS Experimental outcomes–definition of primary and secondary outcomes	0 = no 1 = unclear/not complete 2 = yes
13	METHODS Statistical methods–details and unit of analysis	0 = no 1 = unclear/not complete 2 = yes
14	RESULTS Baseline data–characteristics and health status of animals	0 = no 1 = yes
15	RESULTS Numbers analysed–absolute numbers in each group included in each analysis, explanation for exclusion	0 = clearly inadequate 1 = possibly adequate 2 = clearly adequate
16	RESULTS Outcomes and estimation–results for each analysis with a measure of precision	0 = no 1 = unclear/not complete 2 = yes
17	RESULTS Adverse events–details and modifications for reduction	0 = no 1 = unclear/not complete 2 = yes
18	DISCUSSION Interpretation/scientific implications–study limitations including animal model, implications for the 3Rs	0 = clearly inadequate 1 = possibly adequate 2 = clearly adequate
19	DISCUSSION Generalisability /translation–relevance to human biology	0 = clearly inadequate 1 = possibly adequate 2 = clearly adequate
20	DISCUSSION Funding – sources, role of the funders	0 = clearly inadequate 1 = possibly adequate 2 = clearly adequate

Table 2. Characteristics of the reviewed articles.

Authors	Design	Sample size/Region	Time of assessment	Socket anatomy	Surgical technique (with flap/ flapless)	Characteristics of the created defects	Interventions	Method of measurement	Variable	year
Homayoun H. Zadeh, et al.	RCT	36 patients/61 teeth, anterior maxilla, anterior mandible, premolar, molar	6 months after tooth extraction due to periodontitis, severe caries or failed endodontic treatment	Intact socket/ buccal dehiscence socket	Flapless	NA	A: Control B: KAP C: KAP + ABBM D: Control E: KAP + KAGE + ABBM	Preoperative CBCT/ Preoperative optically laser-scanned cast 6-month postoperative optically laser-scanned cast	Alveolar ridge contour	2016
Alaa AbdelhamidA, et al.	RCT	36 patients/61 teeth, anterior maxilla, anterior mandible, premolar, molar	6 months after tooth extraction due to moderate to severe periodontitis,	Intact socket/ buccal dehiscence socket	Flapless	NA	A: Control B: KAP C: KAP+ ABBM D: Control E: KAP + KAGE + ABBM	Pre OP CBCT 6 month Post OP CBCT	Alveolar bone volume	2016
Omran. Mostafa, et al.	Animal study	48 sockets, Macaca fascicularis non-human primates	6 and 12 weeks after tooth extraction	Intact socket/ buccal dehiscence socket	With flap in sockets with buccal dehiscence	Complete elimination of buccal plate to the apex	A: Control B: KAP C: KAP + ABBM D: Control E: KAGE + ABBM F: KAP + KAGE + ABBM	Pre OP CBCT Post OP CBCT	Alveolar bone volume	2016

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Authors	Design	Sample size/Region	Time of assessment	Socket anatomy	Surgical technique (with flap/ flapless)	Characteristics of the created defects	Interventions	Method of measurement	Variable	year
Kyung-Ho Ryu, et al.	Animal study	6 beagle dogs/24 sockets/ maxillary right and left first premolars, and mandibular right second and fourth premolars	0, 1, 2, 4, 8 and 12 weeks after tooth extraction to assess bone loss, and at 12 weeks for assessment of histological changes	Flapless	NA	A: Control B: KAP C: KAP+KBBM	CBCT Histology, Histomorphometric	Residual bone width, residual bone height, bone density, histological and histomorphometric analysis	Residual bone width, residual bone height, bone density, histological and histomorphometric analysis	2016
Neem-Bakhshalian, et al.	RCT	36 patients/61 teeth, anterior maxilla, anterior mandible, premolar, molar	6 months after tooth extraction due to periodontitis, severe caries or failed endodontic treatment	Intact socket/ buccal dehiscence socket	Flapless	NA	A: Control B: KAP C: KAP + ABBM D: Control E: KAP + KAGE + ABBM	Histology	Quality and quantity of bone, presence of inflammation, percentage of VV, percentage of RG volume, percentage of BV/TV	2018
Yingying Su, et al.	Animal study	6 Macaca fascicularis non-human primates Each with 6 sockets	12 weeks after tooth extraction	Intact socket/ buccal dehiscence socket	Muco-periosteal flap in sockets with buccal dehiscence	Complete elimination of buccal plate from the alveolar crest to apex extending to interproximal line angles	A: Control B: KAP C: KAP + ABBM D: Control E: KAGE + ABBM F: KAP + KAGE + ABBM	CBCT Histology	Residual bone height, residual bone width, histological analysis, assessment of osteogenesis	2017

Authors	Design	Sample size/Region	Time of assessment	Socket anatomy	Surgical technique (with flap/ flapless)	Characteristics of the created defects	Interventions	Method of measurement	Variable	year
Seiko Min, et al.	Animal study	6 Macaca fascicularis non-human primates Each with 6 sockets	6 and 12 weeks after tooth extraction	Intact socket/ buccal dehiscence socket	Muco-periosteal flap in sockets with buccal dehiscence	Complete elimination of buccal plate from the alveolar crest to apex extending to interproximal line angles	A: Control B: KAP C: KAP + ABBM D: Control E: KAGE + ABBM	CBCT	Residual bone width, residual bone height	2016

RCT: Randomized clinical trial; NA: Not available; KAP: SocketKAP, KAGE: SocketKAGE; ABBM: Anorganic bovine bone mineral; CBCT: Cone-beam computed tomography; VV: Void volume; RG: Residual graft material; BV/TV: Bone volume/total volume.

Table 3. Quality Assessment and Potential Risk of Bias of Included RCTs, Based on the Cochrane Risk Assessment Tool.

Criteria/studies	H.Zadeh, et al. 2015	AbdelhamidA,et al. 2015	Bakbsbalian N, et al. 2018
Representative of general population	Yes	Yes	Yes
Allocation concealment method	Yes	Yes	Yes
Examiner masked	Yes	Yes	Yes
Calibration (intraexaminer/ interexaminer)	No	No	No
Defined inclusions/exclusions	Yes	Yes	Yes
Correction for confounding factors	Yes	Yes	Yes
Appropriate statistics methods	Yes	Yes	Yes
All patients accounted for at the end of study	Yes	Yes	Yes
Analysis accounts for patient losses	No	No	No
Estimated potential risk of bias	High	High	High

Table 4. Quality assessment of included animal studies in different categories per checklist item.

Studies/ items	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	total
Omran.M, et al.	1	2	2	0	2	2	2	2	0	0	1	1	2	0	2	2	0	2	1	2	26
Kyung-Ho Ryu, et al.	1	2	2	0	2	2	2	1	0	0	1	1	2	0	2	2	0	2	1	2	25
Min S, et al.	1	2	2	0	2	2	2	2	0	0	1	1	2	0	2	2	0	2	1	2	25
Su Y, et al.	1	2	2	0	2	2	2	2	0	0	1	1	2	0	2	2	0	2	1	2	26

DOI: 10.18502/jcr.v12i3.20621

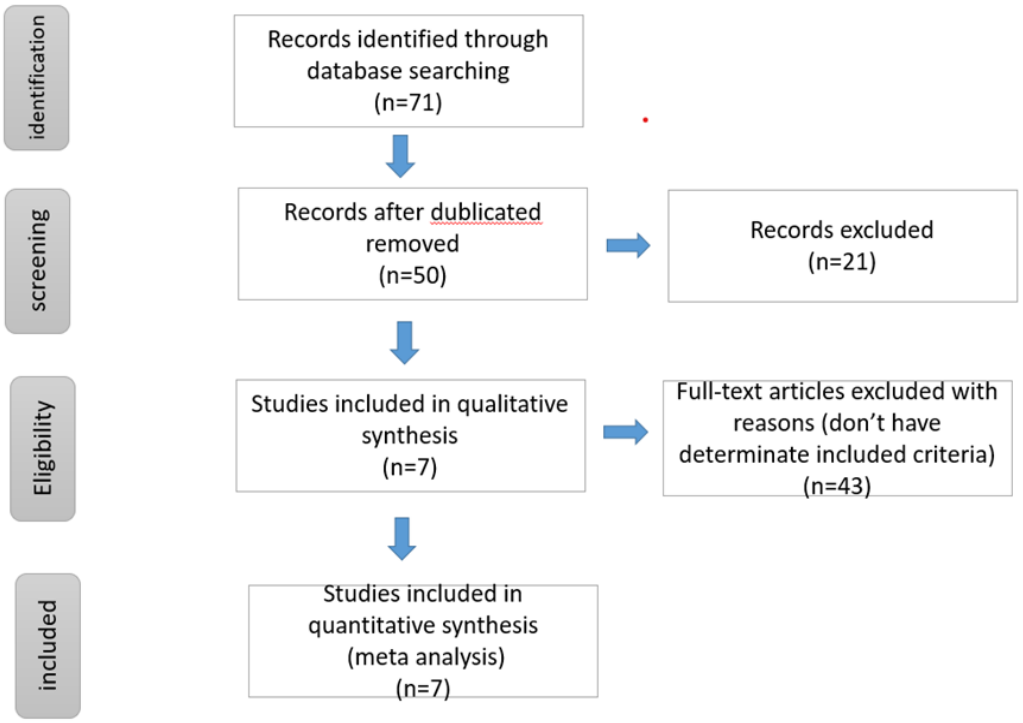

Figure 1. PRISMA flowchart of the study selection process.

Discussion

This systematic review aimed to review studies that assessed the efficacy of SocketKAPTM and SocketKAGETM for the reduction of alveolar ridge changes in tooth extraction sockets. KAP supports the soft tissue collar and prevents the collapse of the gingival margin after tooth extraction. By doing so, it prevents alveolar crest resorption and preserves the alveolar ridge contour [29]. It also seals the opening of the extraction socket. However, the sealing membranes do not have adequate stability without the use of bone fillers and often collapse into the non-grafted sockets [30]. KAP stabilizes the soft tissue and increases the keratinized mucosa covering the tooth socket. KAP minimizes the risk of material contamination by minimizing its exposure to the oral cavity. Its specific design, i.e., presence of a suture channel on the superior surface of the dome, results in placement of sutures before the material, and the socket is sealed after the placement of material [12].

An animal study by Omran et al. [31] showed that at 12 weeks after tooth extraction, treatment with KAP alone only decreased the alveolar ridge volume loss at 3-6mm apical to the alveolar crest, compared with no treatment. In another animal study, Kyung et al. [32] demonstrated that application of KAP alone significantly decreased alveolar width loss at 2 mm apical to the crest in intact sockets at 1 week after tooth extraction, compared with no treatment. Su et al. [23], in their animal study, reported that application of KAP alone significantly decreased the loss of alveolar bone height in intact sockets, compared with no treatment [5]. Min et al. reported that application of KAP alone significantly decreased alveolar bone height loss in the buccal third of intact sockets, compared with no treatment. Thus, in general, all the reviewed studies except for Kyung et. al and Abdelhamid et al. reported that application of KAP alone had additional benefits for alveolar ridge preservation [24].

The addition of biomaterial to extraction sockets improves the ridge morphology and provides adequate socket seal [2]. However, it has drawbacks such as prolonging the socket healing time, higher cost imposed on patients, and the possibility of particles releasing into the socket and the oral cavity [2]. Regarding the efficacy of the addition of material and comparison of KAP+ABBM versus KAP, Zadeh et al. [12] showed that application of KAP+ABBM compared with KAP alone decreased the contour loss at 6-9 mm apical to the crest in intact sockets. In the study by Omron et al. [5] addition of biomaterial to KAP decreased the alveolar bone volume loss at 0-3 mm and 3-6 mm apical to the crest at 6 and 12 weeks after tooth extraction in intact sockets, compared with the control sockets. However, Abdelhamid et al. [6] suggested that the addition of material to KAP did not decrease the alveolar bone

volume loss. In the study by Kyung-Ho et al. [32], application of KAP+ABBM decreased the loss of residual bone height and width in select times and locations. In the study by Su et al. [25], addition of material to KAP decreased the loss of residual bone width and surface compared with the use of KAP alone. In the study by Min et al. [24], treatment with KAP+ABBM decreased socket width loss at 1 and 2 mm apical to the alveolar crest at 6 and 12 weeks after tooth extraction, compared with the use of KAP alone.

Regarding the comparison of KAP+KAGE +ABBM and KAGE+KAP, Su et al. [25] reported that the addition of ABBM to KAGE+KAP significantly decreased the loss of alveolar bone width and surface. In the study by Min et al. [24], addition of ABBM to KAGE+KAP decreased alveolar width loss at 3 mm apical to the alveolar crest at 6 weeks, and at 2, 3, and 5 mm apical to the crest at 12 weeks. Also, it decreased bone height loss in the middle third at 6 weeks and in the buccal third at 12 weeks after tooth extraction. Regarding the simultaneous use of KAP and KAGE versus KAGE, Omron et al. [5] reported that alveolar bone volume loss was lower at 0-3 and 3-6 mm apical to the crest in sockets with buccal dehiscence treated with KAP+KAGE at 6 and 12 weeks, compared with treatment with KAGE alone. Regarding the PLLA residues derived from the prefabricated KAGE device, Bakhshalian et al. [2], in their clinical study, reported that no PLLA residues were noted at 6 months after treatment with KAP+KAGE+ABBM. Two possible hypotheses have been suggested for this finding: **(I)** the buccal position of KAGE in the socket and location of biopsy determined by implant placement, which is mainly lingual or palatal, and **(II)** resorption of KAGE over time. However, in the animal study by Su et al. [25], histological sections in the KAGE treatment group showed PLLA residues. Thus, since implants are not intended to be placed in animal studies, and biopsy is obtained from a more buccal position, the hypothesis regarding the resorption of KAGE over time is less likely; while the hypothesis regarding the effect of location of biopsy on the presence of PLLA residues is more likely to be true. Regarding the inflammatory response and infiltration in response to KAP and KAGE, Bakhshalian et al [30], in their histological study, reported no inflammatory infiltration in response to application of KAP and KAGE. Su et al. [25] did not report any evidence of inflammatory response in the biopsy specimens of the sockets treated with KAGE+KAP and KAGE+KAP+ABBM. Kyung-Ho et al. [32] reported that in the clinical setting, mild inflammation was noted in patients after placement of KAP and KAGE, but there was no infection. Thus, it seems that the tissue response is favorable to KAP and KAGE. Several factors, such as single or multiple tooth sockets, type of extracted tooth (anterior/posterior), jaw (maxilla/mandible), reason for tooth loss, and flap or flapless surgery, affect the results of ridge preservation with the use of KAP and KAGE. Regarding single or multiple tooth extraction sockets, Abdelhamid et al. [6] and Zadeh et al. [12] reported higher ridge contour resorption when there were several tooth extraction sockets; however, the difference was not significant. They reported the reason to be their small sample size. Previous studies reported maximum bone remodeling when there were several tooth extraction sockets [28].

Zadeh et al. [12] and Abdelhamid et al. [6] reported higher frequency of buccal dehiscence in the anterior region, especially in the anterior maxilla, and reported the reason to be periodontal disease in most cases. However, Omron et al. [5] reported that tooth position was the main reason for the thinness of the buccal plate and subsequently the high prevalence of buccal dehiscence. Thus, it may be concluded that the location of the socket, especially in the anterior region, can be a confounding factor. Regarding the technique of surgery, Zadeh et al. did not elevate a flap; they reported the reason to be the possibility of higher bone resorption following flap elevation according to the previous literature [12]. However, animal studies. [24] elevated a flap to create a buccal defect in cases with buccal dehiscence. Although the abovementioned factors can cause heterogeneity in the results of studies, the samples better represent the cases commonly encountered in the clinical setting.

Conclusion

KAP alone and KAP+Anorganic bovine bone mineral (ABBM) significantly decreased contour loss in human intact sockets compared with no intervention. KAP+ABBM significantly decreased alveolar bone volume loss in human intact sockets compared with no intervention. KAGE+KAP+ABBM significantly decreased contour loss and alveolar bone volume loss in human sockets with dehiscence compared with no intervention. KAP alone and KAP+ABBM significantly decreased the alveolar bone volume loss, width loss and height loss of non-human intact sockets compared with no treatment. KAGE+KAP+ABBM and KAP+KAGE were more effective than no treatment in reducing the alveolar bone volume loss, width loss and height loss in non-human sockets with dehiscence. According to the findings of this review study, **(I)** future studies with

DOI: 10.18502/jcr.v12i3.20621

longer follow-ups and larger sample sizes are required on the efficacy of KAP and KAGE; **(II)** confounding factors should be eliminated or standardized to assess the actual effect of KAP and KAGE (standardization of the groups); **(III)** other ridge preservation protocols and materials and the conventional methods should be compared with the application of KAP and KAGE. Within the Limits of the review, KAP and KAGE might be beneficial for decreasing the alveolar ridge changes, given as to whether the cost-effectiveness is justifiable.

Acknowledgment

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest

There is no conflict of interest to declare.

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