Review

An Evaluation of Bioactive Glass in the Treatment of Periodontal Defects: A Meta-Analysis of Randomized Controlled Clinical Trials

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Background: The regenerative surgical treatment of intrabony defects caused by periodontal disease has been examined in several systematic reviews and meta-analyses. The use of bioactive glass (BG) as a graft material to treat intrabony defects has been reported, but all data have not been synthesized and compiled. Our objective was to systematically review the literature on the use of BG for the treatment of intrabony defects and to perform a meta-analysis of its efficacy.

Methods: A search of PubMed, EMBASE, and Cochrane Database of Systematic Reviews, as well as a manual search of recently published periodontology journals, were conducted to identify randomized controlled trials of the use of BG in the treatment of intrabony and furcation defects. Criteria included publication in English, follow-up duration of ≥6 months, baseline and follow-up measures of probing depth (PD) and clinical attachment levels (CAL) with 95% confidence intervals (CIs), and an appropriate control arm. Twenty-five citations were identified, 15 of which were included in the final analysis. Data, including study methods and results, as well as CONSORT (Consolidated Standards of Reporting Trials) criteria, were extracted from eligible studies and cross-checked by at least two reviewers.

Results: Meta-analyses of eligible studies were performed to ascertain summary effects for changes in PD and CAL among experimental and control groups, using the mean change plus standard deviation for each study. Pooled analyses showed that BG was superior to control for both measures: the mean (95% CIs) difference from baseline to follow-up between BG and controls was 0.52 mm (0.27, 0.78, $P<0.0001$) in reduction for PD and 0.60 mm (0.18, 1.01, $P=0.005$) in gain for CAL. Analyses of CAL revealed heterogeneity across studies ($I^2=60.5\%$), although studies reporting PD measures were homogeneous ($I^2=0.00\%$). CAL heterogeneity appeared secondary to active controls versus open flap debridement (OFD) alone and to defect-type modifying BG treatment success. Per subgroup analyses, the benefit of BG over control treatment was highly significant only in studies comparing BG to OFD ($P<0.0001$), with mean difference change in CAL being 1.18 mm (95% CI = 0.74, 1.62 mm) between the BG and OFD group.

Conclusion: Treatment of intrabony defects with BG imparts a significant improvement in both PD and CAL compared to both active controls and OFD. *J Periodontol 2012;83:453-464.*

KEY WORDS

Bioglass; furcation defects; meta-analysis; periodontal diseases; randomized controlled trial.

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Periodontal disease is characterized by the loss of connective tissue attachment and alveolar bone that support the teeth.[1,2] Specific periodontal pathogens cause a host-mediated response that can result in the loss of the tooth-supporting tissues.[3] Clinically, the disease results in the formation of soft-tissue pockets or deepened crevices between the gingiva and tooth root.[1] If these sites of deterioration are left untreated, loss of supporting bone will occur, resulting in the formation of intraosseous or furcation defects. There is strong evidence that these defects are associated with an increased risk for continued loss of periodontal attachment and disease activity.[4,5]

Bone replacement grafts remain among the popular therapeutic modalities for the treatment of periodontal defects. A wide range of graft materials, including autografts, allografts, xenografts, and synthetic materials, have been used for the treatment of intrabony and furcation defects.[6-10] One of the synthetic grafts, bioactive glass (BG), developed by Hench et al. in the late 1960s,[11] has been used for the treatment of intrabony periodontal defects. BGs release soluble silicon, calcium, phosphorus, and sodium ions that lead to cellular responses at the interface of the glass and bone.[12] This interaction induces osteoconduction and osteoinduction[13-16] and results in the formation of a hydroxyapatite layer that has a stiffness closely matching the mineral phase of bone[16] without forming fibrous tissue or promoting inflammation or toxicity. The high biocompatibility and reactivity of these glasses has been identified as their main advantage for their application in periodontal repair and bone augmentation.[17,18]

Although there has been little human histologic evidence to show bone regeneration or formation of new connective tissue attachment, there is a large amount of experimental data supporting the application of BG in a variety of clinical applications, including sinus augmentation, ridge preservation, and treatment of various bony defects in humans.[19-33] Although BGs have been widely used in the treatment of periodontal defects,[28-48] their clinical benefit requires clarification through a systematic review of randomized controlled trials (RCTs). To the best of our knowledge, the last systematic review of RCTs on the role of BGs in the treatment of osseous defects was performed in 2002 on only four studies.[49] The publication of several recent RCTs on BGs since the release of the last systematic review necessitates a new comprehensive review and meta-analysis. The aim of the present review is to systematically review the literature on the use of BG compounds for intrabony and furcation defects in periodontal disease and to perform a meta-analysis of the efficacy and effectiveness of this material in the regenerative treatment of intrabony defects.

MATERIALS AND METHODS

Search Strategy and Eligibility Criteria

PubMed, EMBASE, and Cochrane Database of Systematic Reviews were searched for all peer-reviewed, RCTs evaluating use of BG in treating periodontal defects. Searches were not restricted by publication date. Both keywords and MeSH terms were used in the PubMed search (Table 1). In addition to these databases, the reference lists of articles obtained by the electronic search, reference lists of review articles, and major periodontology journals (*Journal of Periodontology*, *Journal of Clinical Periodontology*, *Journal of Periodontal Research*, and *The International Journal of Periodontics and Restorative Dentistry*) were searched manually for relevant articles. During the review process, we contacted experts and companies involved in this area of research to find other trials or unpublished material or to clarify ambiguous or missing data. To be included in this analysis, studies were required to: 1) be RCTs; 2) be conducted on human teeth; 3) be English-language publications; 4) have ≥6 months of follow-up by surgical reentry; 5) include pretreatment and post-treatment probing depth (PD) and/or clinical attachment level (CAL) measures or report the changes in these parameters; and 6) report mean and standard deviation or standard error of outcome values.

Titles and abstracts, and full texts when necessary, were screened for eligibility and confirmed by a second reviewer. In the case of discord among reviewers, consensus was reached by discussion. After screening, 11 studies were excluded from the CAL analysis and 12 were excluded from the PD analysis (Fig. 1). Reasons for exclusion were: 1) review article (n = 2); 2) inadequate control group (n = 2); 3) duplicate study (n = 2); 4) animal study (n = 1); 5) non-English study (n = 1); and 6) omission of change in CAL and/or PD between baseline and follow-up (n = 3 to 4). A total of 15 studies were left for the final analysis.

Data Extraction

Data extraction was performed independently for each eligible study by at least two reviewers (KS, VS, TAL, MH, MB) using a standardized form. The following variables were extracted from each study: 1) study outcomes (PD, CAL); 2) study design (randomized split-mouth design, randomized parallel trial); 3) patient demographics (age, sex, ethnicity, socioeconomic status, comorbidities); 4) inclusion and exclusion criteria; 5) year of publication; 6) setting and country of intervention; 7) funding sources; 8) trial duration; 9) treatment and control interventions; 10) additional exposures; 11) number of participants in treatment and control groups; 12) number of teeth in treatment and control groups; and 13) occurrence of adverse effects. We also collected data on each of

Table 1.

Characteristics of Studies and Participants Included in Meta-Analysis

Citation	Country	Treatment	Control	Study Design	Sample Size	Defect Type	Age (Years)	% Male	Trial Duration	Measured Outcomes*
Subbaiah and Thomas (2011)[37]	India	BG	OFD	Randomized split mouth	8 Participants 16 Teeth	Intrabony defects	NR	NR	9 months	PD and CAL
Leknes et al. (2009)[38]	Norway	BG	EMD	Randomized split mouth	13 Participants 26 Teeth	Intrabony defects	Mean, 52.5	NR	12 months	PD and CAL
Dybvik et al. (2007)[39]	Norway	BG	OFD	Randomized parallel trial	19 Participants 19 Teeth	Intrabony defects	Mean, 54.4	68	12 months	PD and CAL
Keles et al. (2006)[40]	Turkey	BG + GTR	PP + GTR	Randomized split mouth	15 Participants 30 Teeth	intrabony defects	Mean ± SD, 39.1 ± 7.4	53	6 months	CAL
Kuru et al. (2006)[41]	Turkey	BG + EMD	EMD	Randomized parallel trial	23 Participants 30 Teeth	Intrabony defects	Mean, 44.7	NR	8 months	PD and CAL
Sculean et al. (2005)[42]	Netherlands	BG + EMD	EMD	Randomized parallel multicenter	30 Participants 30 Teeth	Intrabony defects	NR	47	1 year	PD and CAL
Mengel et al. (2003)[43]	Germany	BG	GTR	Randomized split mouth	12 Participants 30 Teeth	Intrabony defects	Range, 34 to 59	25	12 months	PD and CAL
Park et al. (2001)[35]	Korea	BG	OFD	Randomized parallel trial	38 Participants 38 Teeth	Intrabony defects	Mean ± SD, 43.9 ± 9.0	62	6 months	PD and CAL
Yukna et al. (2001)[44]	United States	BG	GTR	Randomized split mouth	27 Participants 54 Teeth	Furcation defects	Mean, 54; range, 39 to 72	41	6 months	PD and CAL
Rosenberg et al. (2000)[45]	United States	BG	OFD	Randomized split mouth	12 Participants 12Teeth	Intrabony defects	Mean, 41	50	6 months	CAL
Anderegg et al. (1999)[46]	United States	BG	OFD	Randomized split mouth	15 Participants 30 Teeth	Furcation defects	Mean, 55; range, 42 to 67	40	6 months	PD
Froum et al. (1998)[47]	United States	BG	OFD	Randomized split mouth	16 Participants 59 Teeth	Intrabony or furcation defects	Mean, 43	50	12 months	PD and CAL
Lovelace et al. (1998)[48]	United States	BG	DFDBA	Randomized split mouth	15 Participants 30 Teeth	Intrabony defects	Mean, 45; range, 30 to 63	40	6 months	PD and CAL

Table 1. (continued)

Characteristics of Studies and Participants Included in Meta-Analysis

Citation	Country	Treatment	Control	Study Design	Sample Size	Defect Type	Age (Years)	% Male	Trial Duration	Measured Outcomes*
Ong et al. (1998)[34]	United States	BG	OFD	Randomized split mouth	14 Participants 27 Teeth	Intrabony defects	Mean, 49.1; range, 35 to 67	78.5	9 to 13 months	PD and CAL
Zamet et al. (1997)[36]	United Kingdom	BG	OFD	Randomized split mouth	22 Participants 44 Teeth	Intrabony defects	Mean ± SD, 39.6 ± 9.6	45.5	12 months	PD and CAL

NR = not reported.
* Measured outcomes includes those outcomes relevant for this meta-analysis (PD and CAL).

the CONSORT (Consolidated Standards of Reporting Trials) criteria to evaluate study quality.[50]

Statistical Analyses

We compared change from baseline between treatment and control for both PD and CAL. Meta-analyses were conducted for each outcome with a random-effects model.[51] Weighted mean differences (WMDs) were calculated because the measurements used to assess study outcomes were highly homogeneous across studies.[52] Heterogeneity across studies was assessed with the I^2 statistic.[53] Publication bias was evaluated with Begg and Egger tests, as well as with examination of Egger and funnel plots.[52]

Sensitivity analyses were conducted, evaluating the pooled effect estimates after omitting each study individually, to determine the effect of individual studies on the overall mean difference. Heterogeneity across studies was evaluated with meta-regression and subgroup analyses.[52] Potential sources for heterogeneity that were examined by way of subgroup analysis were study design (split mouth versus parallel), defect (intrabony versus furcation), control intervention (open flap debridement [OFD], enamel matrix protein derivative [EMD], guided tissue regeneration [GTR], demineralized freeze-dried bone allograft [DFDBA], and platelet pellet [PP]), and treatment intervention (BG alone versus BG plus another active treatment). All analyses were conducted with statistical software.§

RESULTS

Description of Studies

The PubMed search yielded 25 citations, and the EMBASE search returned 22 citations, all of which were duplicates of citations identified through PubMed. The Cochrane Database of Systematic Reviews returned zero publications. We did not identify any additional trials through our manual searches (Fig. 1).

Fifteen studies were included in this meta-analysis (Table 2); 13 contributed to the PD analysis, and 14 contributed to the CAL analysis. In total, this meta-analysis included 252 participants with 426 teeth with PD measurements and 264 participants with 438 teeth with CAL measurements. The majority of studies were of patients with intrabony defects; two studies were of patients with furcation defects, and another study included patients with both intrabony and furcation defects. Eleven of the 15 studies were randomized split-mouth designs; the remaining four studies were randomized parallel trials. The mean ages of the participants ranged from 39 to 55 years, and 25% to 78% of the participants in the studies were male. Eight of the studies compared BG to OFD, and the remaining seven studies used active controls, including EMD,

§ Stata version 11, StataCorp, College Station, TX.

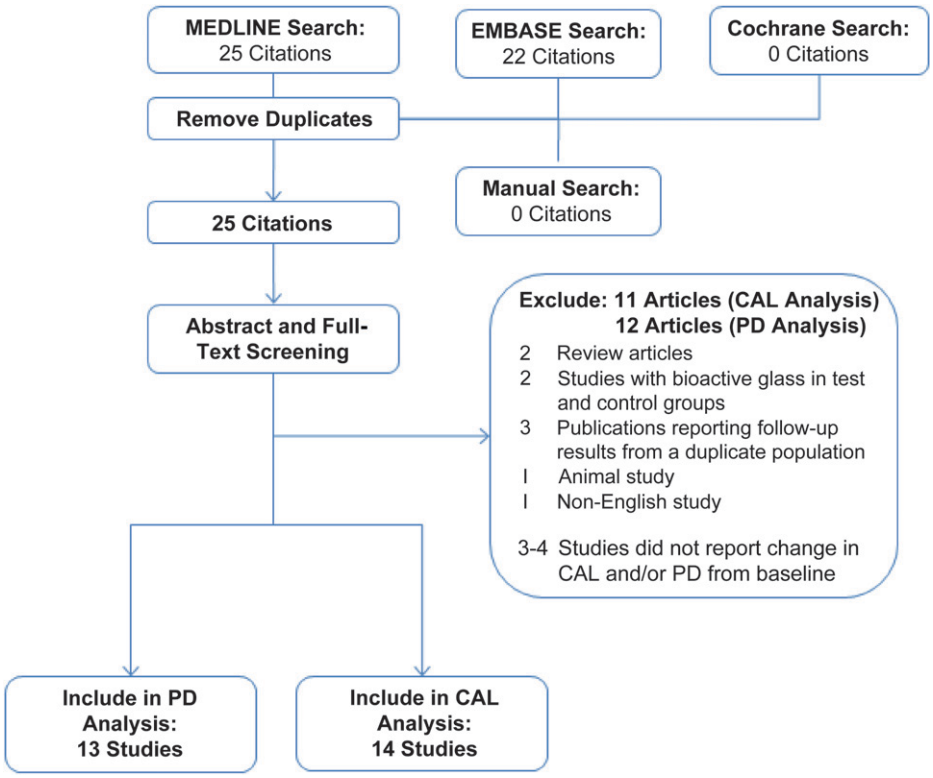

Figure 1.
Description of systematic literature search.

GTR, DFDBA, and PP. Three of these studies compared BG plus an active treatment to the active treatment alone.

Meta-Analysis and Assessment of Bias and Effect Modification

Pooled analyses showed that BG was superior to controls for both PD and CAL. The mean (95% confidence intervals [CI]) difference between BG and controls in change in PD from baseline to follow-up was 0.52 mm (0.27, 0.78, P <0.0001) (Fig. 2). The mean (95% CI) difference between BG and controls in change in CAL from baseline to follow-up was 0.60 mm (0.18, 1.01, P= 0.005) (Fig. 3). Studies were homogeneous with respect to changes in PD (I^2 = 0.00%), but they were heterogeneous with respect to CAL (I^2 = 60.5%). This indicates a high level of heterogeneity in the CAL analysis (heterogeneity χ^2, P= 0.002). Factors responsible for study heterogeneity were explored in subgroup analyses.

There was borderline evidence of publication bias among estimates of change in PD (Egger test, P = 0.08; Begg test, P = 0.05). However, during examination of the funnel plot, this appears to be driven primarily by one study.[39] This study was only given a weight of 2.08% and did not dramatically alter the pooled estimate in sensitivity analysis, so we do not believe that it biased the overall estimate. Among studies reporting changes in CAL, there was no evidence of publication bias (Egger test, P = 0.84; Begg test, P = 0.96). For the CAL estimates, the Egger plot had a nearly 0 intercept, and the funnel plot did not show any obvious asymmetry.

Per sensitivity analyses, exclusion of any single study significantly altered results for either PD or CAL. Exclusion of the study[47] that combined furcation defects with intrabony defects had the largest impact, reducing the estimate for PD to 0.45 mm (95% CI = 0.18, 0.72 mm) and for CAL to 0.47 mm (95% CI = 0.11, 0.84 mm), but the CIs for difference in mean change of both PD and CAL after omission of this study overlapped substantially with the CIs of the full pooled effects (PD 95% CI = 0.27, 0.78 mm; CAL 95% CI = 0.18, 1.01 mm).

Subgroup Analyses

Papers reporting change in PD were homogeneous, and subgroup analyses were consistent with homogeneity across study designs, defect types, control interventions, and treatment interventions (Table 2). However, after restriction, studies using a parallel design, control intervention other than OFD, or BG plus another material as the treatment intervention were no longer significant, most likely because of small sample sizes. In papers reporting CAL, there were not significant differences by study design (P = 0.90) or treatment intervention (P = 0.34). However, after restriction, studies using a parallel design or BG plus another material as the treatment intervention were no longer significant. When restricting by control type, only studies using OFD as the control technique were statistically significant (P<0.0001) (Figs. 4 and 5). In these studies, mean change in CAL was 1.18 mm (95% CI = 0.74, 1.62 mm). Mean changes in CAL in studies using EMD, GTR, DFDBA, or PP were estimated to be 0.41, 0.03, 0.40, and 0.00 mm, respectively, none of which were significantly different from 0. In studies limited to intrabony defects, mean change in CAL was 0.54 mm (95% CI = 0.14, 0.94), and mean change in PD was 0.40 (95% CI = 0.06, 0.74) (Figs. 6 and 7).

Table 2.

Subgroup Analyses

Subgroups	# of Studies	PD			CAL		
		WMD	95% CI	*P* Value*	WMD	95% CI	*P* Value*
Study design							
Parallel design	4	0.34	(–0.27, 0.96)		0.62	(–0.26, 1.51)	
Split mouth	11	0.56	(–0.27, 0.85)	0.64	0.58	(0.084, 1.07)	0.90
Defect type							
Intrabony	3	0.40	(0.083, 0.67)		0.47	(0.11, 0.83)	
Furcation†	12	0.69	(0.44, 1.42)	0.085	1.73‡	(1.08, 2.38)	0.043
Control type							
OFD	8	0.72	(0.36, 1.08)		1.18	(0.74, 1.62)	
EMD	3	0.35	(–0.21, 0.91)	0.30	0.41	(–0.68, 1.50)	0.21
GTR	2	0.22	(–0.34, 0.79)	0.18	0.029	(–0.45, 0.51)	0.043
DFDBA	1	0.50†	(–0.32, 1.32)	0.64	0.40‡	(–0.40, 1.20)	0.29
PP	1	NR			0.00‡	(–0.70, 0.70)	0.10
Treatment type							
BG alone	12	0.54	(0.26, 0.81)		0.72	(0.25, 1.19)	
BG + intervention	3	0.33	(–0.61, 1.28)	0.82	0.21	(–0.75, 1.18)	0.34

NR = not reported.
* χ^2 test derived from meta-regression model.
† Furcation defects with or without intrabony defects.
‡ Estimate reported from single study.

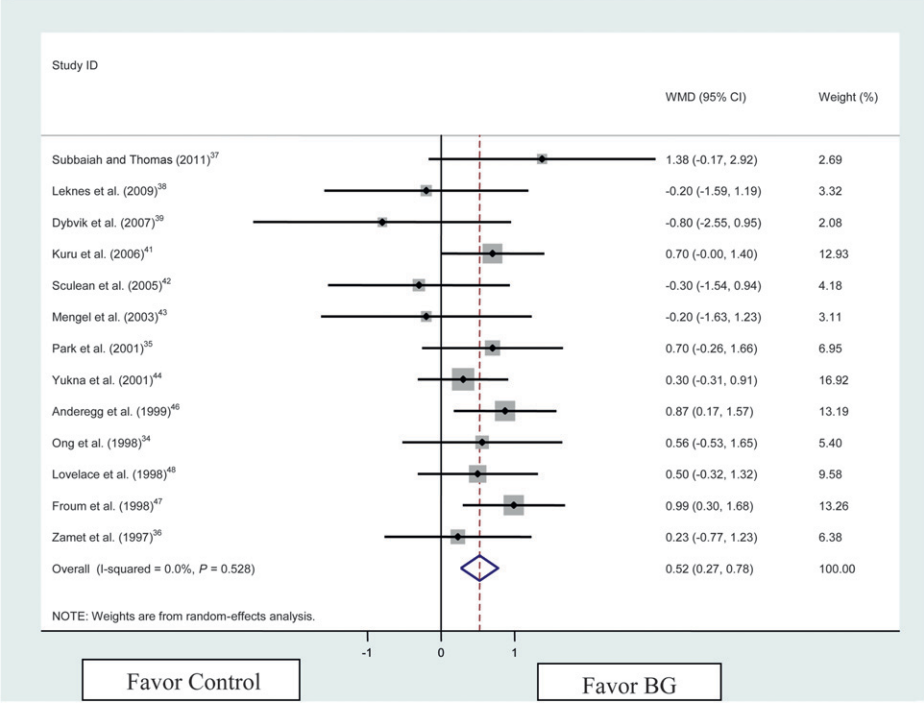

Figure 2.
Forest plot comparing mean PD difference between BG and controls. Squares represent the WMD (in millimeters) in PD for BG versus controls. Size of the squares is proportional to the study weight of the trials. Error bars represent 95% CIs. The diamond represents the pooled estimates within each analysis. P values in this figure represent significance levels for the degree of heterogeneity across the studies in this analysis.

DISCUSSION

There have been several RCTs in the dental literature that have evaluated BG and its efficacy in the treatment of periodontal intraosseous defects. To our knowledge, this systematic review and meta-analysis of the efficacy of BG in the treatment of periodontal defects is the first since 2002.[49] Because there have been several new publications on BG since the last systematic review, our investigation summarizes new evidence and reevaluates the efficacy of BG in the treatment of periodontal intraosseous defects.

In this investigation, efficacy was defined as reduction in PD and gain in CAL when comparing treatment and control groups. We found support for the use of BG in the treatment of intraosseous defects, with PD reduction of 0.52 mm (0.27, 0.78) and CAL gain of 0.60 mm (0.18, 1.01). Traditionally, OFD has been the standard of care for management of

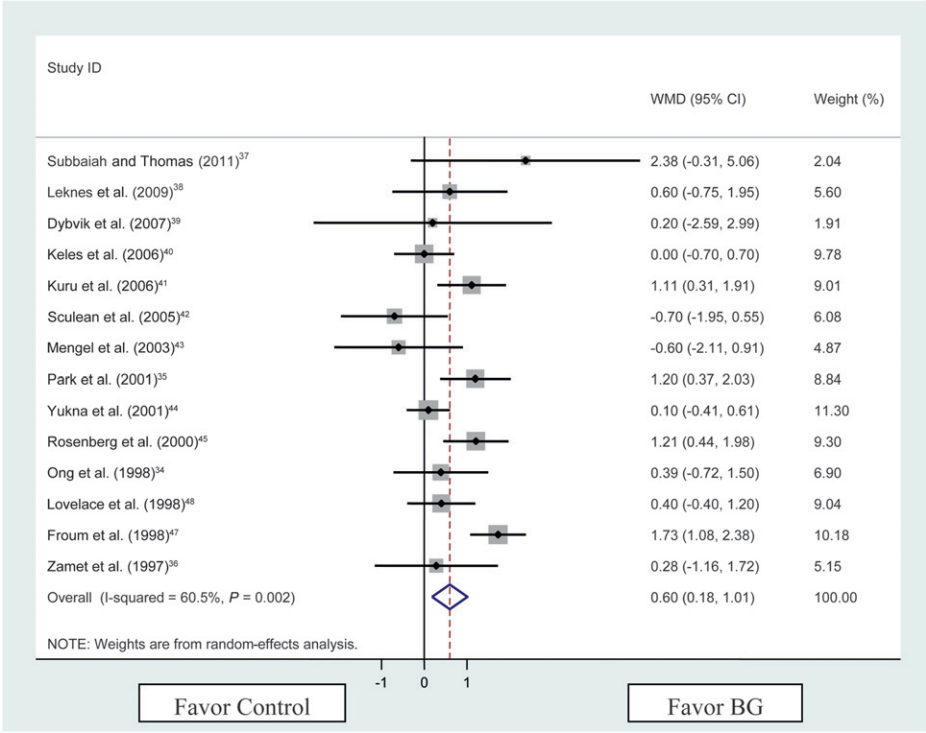

Figure 3.
Forest plot comparing mean CAL difference between BG and controls. Squares represent the WMD (in millimeters) in PD for BG versus controls. Size of the squares is proportional to the study weight of the trials. Error bars represent 95% CIs. The diamond represents the pooled estimates within each analysis. P values in this figure represent significance levels for the degree of heterogeneity across the studies in this analysis.

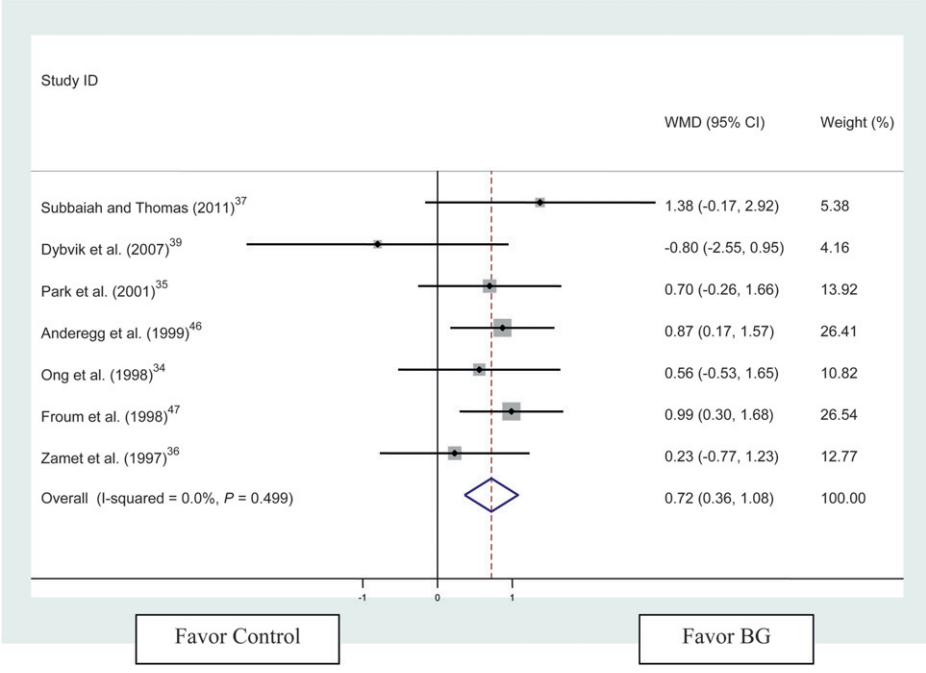

Figure 4.
Forest plot comparing mean PD difference between BG and OFD. Squares represent the WMD (in millimeters) in PD for BG versus controls. Size of the squares is proportional to the study weight of the trials. Error bars represent 95% CIs. The diamond represents the pooled estimates within each analysis.

intrabony defects and is used as the gold standard for comparison against other regenerative treatment modalities in clinical trials. In our subgroup analysis looking at individual comparisons between BG and other treatment modalities, we found a significant improvement in both PD reduction and CAL gain in the comparison between BG and OFD; BG compared to treatments with other regenerative materials (EMD, GTR, DFDBA, and PP) was not statistically different. A subgroup analysis of BG treatment against OFD (placebo) identified CAL gain of 1.18 mm (95% CI = 0.74, 1.62 mm) and pocket reduction of 0.72 (0.36, 1.08), suggesting a favorable and clinically significant benefit of BG in the treatment of bony defects compared to placebo.

The previous systematic review of literature of the efficacy of BG for the treatment of periodontal intraosseous defects found a significant improvement in CAL gain of 1.04 mm (95% CI = 0.31, 1.76 mm), which is very similar to the result of our subgroup analysis.[49] In our analysis, CAL gain was still found to be statistically significant but was attenuated to 0.60 mm (95% CI = 0.18, 1.01 mm). This mitigation of CAL gain can be explained by the fact that our pooled estimate includes a number of studies comparing BG to active controls. The meta-analysis performed by Trombelli et al.[49] included only studies comparing BG to OFD (inactive treatment). As noted previously, the estimate from the previous systematic review was based on only four studies, whereas our data were compiled from 15. In addition, we investigated both PD reduction as well as CAL gain, whereas the previous systematic review evaluated improvement in CAL only.[49]

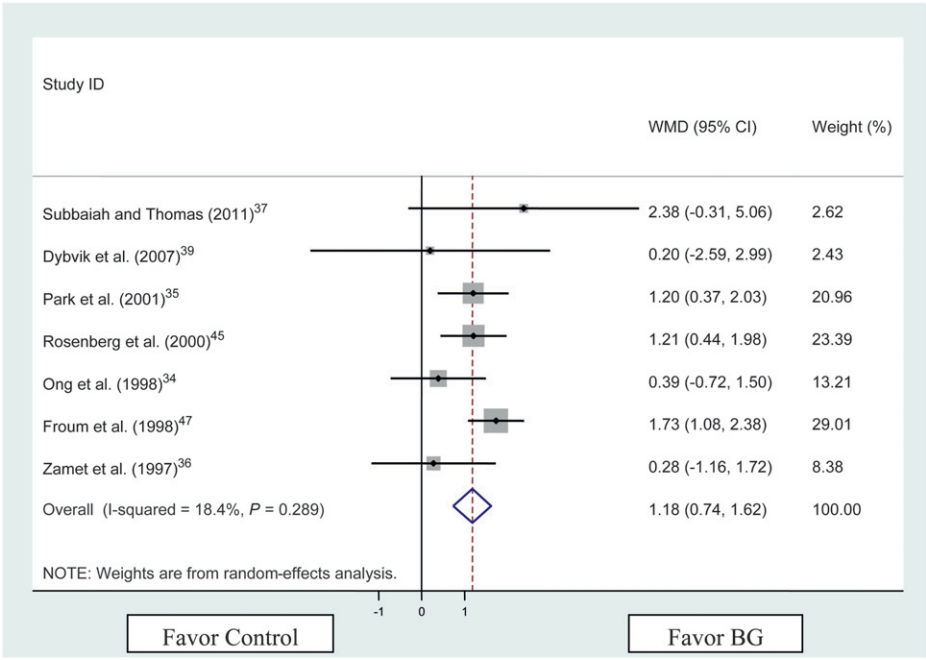

Figure 5.
Forest plot comparing mean CAL difference between BG and OFD. Squares represent the WMD (in millimeters) in PD for BG versus controls. Size of the squares is proportional to the study weight of the trials. Error bars represent 95% CIs. The diamond represents the pooled estimates within each analysis.

Evaluation of study quality revealed several potential sources of bias in the studies included in this meta-analysis. Several reports did not explain the method of randomization, allocation concealment, or masking of therapist and examiners. Assumptions and simplifications included accepting the authors' statement of randomization because this was rarely described in detail. Allocation concealment was not described for any trial and was assumed to have consisted of the author enrolling a participant and then creating the randomization "on the spot," because those studies in which randomization was described performed it by a coin flip. Nine of 15 studies were randomized by a coin flip after enrolling the participants,[38-43,46-48] one study by the roll of a die,[44] one study by "drawing a coded paper from a paper bag,"[34] and four studies did not specify the method of randomization.[35-37,45]

Bias was assessed by attempting to ascertain the degree of masking. Nine of 15 studies described the use of an evaluator who was masked to the treatment group assignment in assessing the clinical measurements at follow-up.[34-36,38-41,43,47] Six studies did not report any masking,[37,42,44-46,48] and one of these studies reported that all the treatments and measurements were performed by the sole investigator.[46]

When funding was received from commercial companies whose products were used in the study, the authors did not note this as a potential source of bias. Six studies did not specifically make a conflict of interest statement or identify the presence or absence of outside supporting funds.[35,37,39-41,46] Two of the three authors of one paper were employees of the pharmaceutical company that manufactured the BG product‖ used in the study,[46] and a second paper also had a coauthor who was employed by the manufacturer of the BG product¶ used in the study, as well as being supported by a grant from the company.[45] Only one study[38] specifically stated, "The authors report no conflicts of interest related to this study. The study was self-funded by the authors and their institutions."

All evaluated BG materials#,**,†† in the included studies appeared to be bio-compatible, and there were no reports of adverse effects, such as allergies or other immunologic reactions, abscess formation, or rejection of the grafting materials. The main limitation inherent in the BG products that are currently available is that they are granular in nature and, as such, cannot serve reliably as space-making materials. Despite this restriction of use, they exhibit the ability to bond to bone and can be used to deliver osteopromotive growth factors.[54,55] The range of applications of BG could be extended within the scope of periodontal regenerative therapy if the material could be redesigned to offer space-making properties. Incorporation or coating with osteogenic agents, such as growth factors, may also be worthwhile.[54,55]

For this review, publication bias was investigated and found not to be statistically significant. Although it should be acknowledged that such tests are conservative in their ability to demonstrate bias,[56] the number of studies included should have been sufficient to identify publication bias if it was present.

Data from the included studies allowed us to investigate some clinical aspects that could affect heterogeneity in the analysis. These included defect types (furcation or intrabony), control interventions (OFD, EMD, GTR, DFDBA, PP), and design of the study (split mouth or parallel). Study design was considered in the subgroup analysis because it has been speculated that protection

‖ PerioGlas, Block Drug Company, Jersey City, NJ.
¶ BioGran, Orthovita, Malvern, PA.
# BioGlass, US Biomaterials, Alachua, FL.
** PerioGlas, Block Drug Company.
†† BioGran, Orthovita.

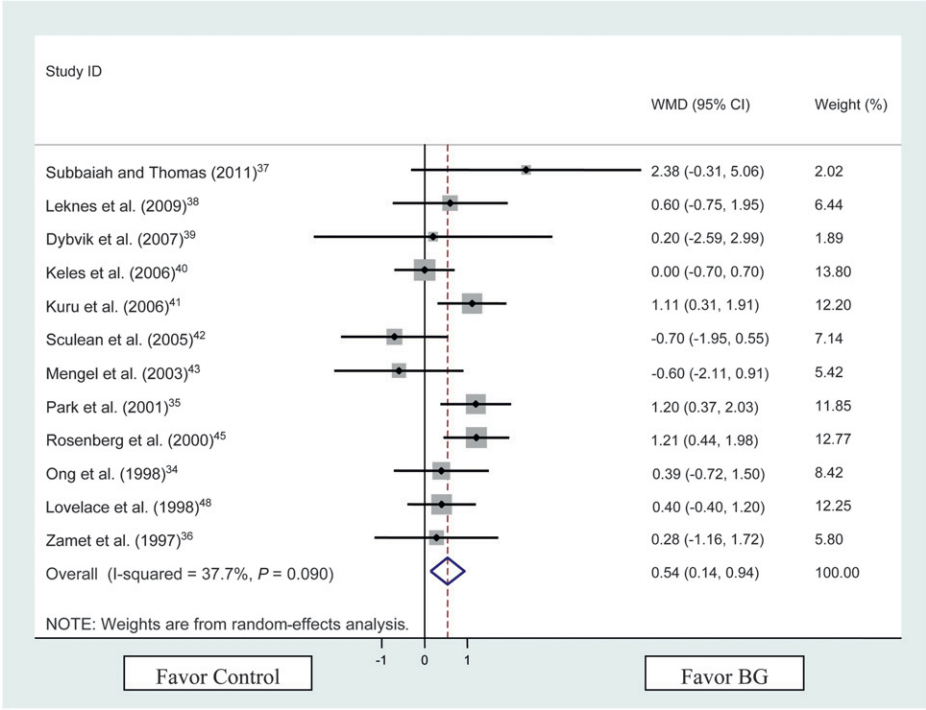

Figure 6.
Forest plot comparing mean CAL difference between BG and controls in intrabony defects. Squares represent the WMD (in millimeters) in PD for BG versus controls. Size of the squares is proportional to the study weight of the trials. Error bars represent 95% CIs. The diamond represents the pooled estimates within each analysis.

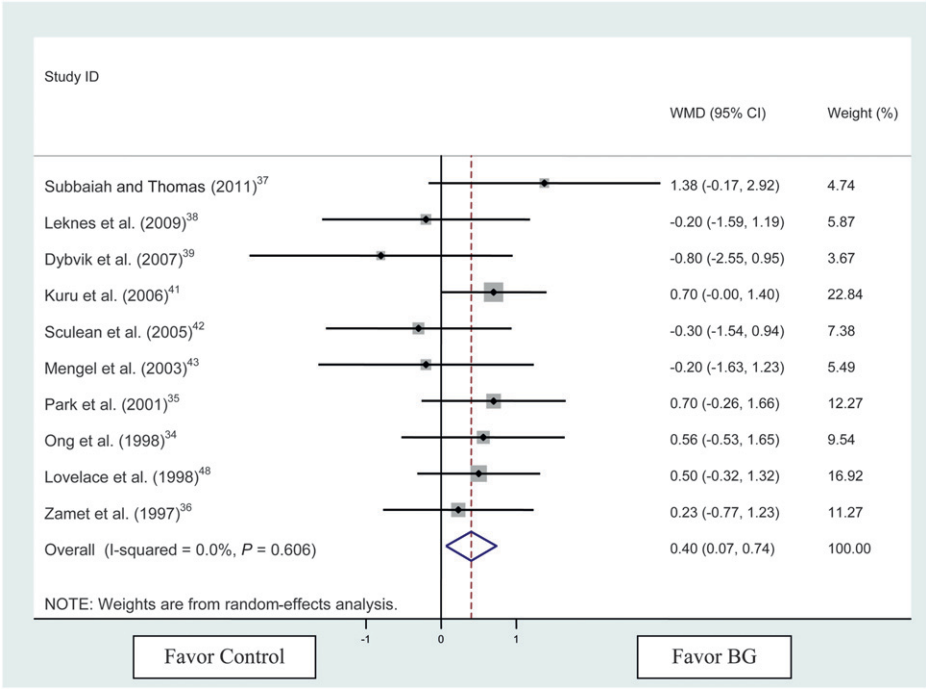

Figure 7.
Forest plot comparing mean PD difference between BG and controls in intrabony defects. Squares represent the WMD (in millimeters) in PD for BG versus controls. Size of the squares is proportional to the study weight of the trials. Error bars represent 95% CIs. The diamond represents the pooled estimates within each analysis.

from bias could be more likely in split-mouth studies.[57] For instance, selection bias might be a lesser risk because the patient provides both experimental groups. In addition, split-mouth studies might help in maintaining the masking of patient, clinician, and examiner.[57] Conversely, crossover effect is not negligible in split-mouth studies, and this effect could reduce the difference in outcome between interventions and shift the result toward the null.[58] Our analysis demonstrated no statistically significant difference between parallel group and split-mouth design studies with respect to CAL gain and PD reductions.

An explanation for the heterogeneity in CAL measurements might be variability between studies in prognostic factors that have been demonstrated to affect the outcome of periodontal regenerative surgery. These factors include, but are not limited to, patient-related factors, such as smoking, compliance with oral hygiene instructions, residual inflammation after cause-related therapy, presence of systemic diseases and comorbidities, plaque levels, defect severity, and surgical skill and experience of the operator.[59] Regarding plaque and smoking, it is apparent that differences in the way both factors are mentioned among different investigations prevent analytical comparison. As an example, some studies present full-mouth plaque scores, other investigations present plaque scores at special sites, and some other studies present no plaque data. Therefore, the extent to which we can successfully address the heterogeneity issue might be limited. Smoking has well-documented deleterious effects on the periodontal status and regenerative treatments,[59-62] but most

of the studies included herein did not report adequate data regarding patient smoking status.

Despite these shortcomings, this analysis suggests a clinical benefit of using BG in the treatment of intraosseous defects, particularly compared to placebo (OFD). When comparing BG to EMD (three trials) and BG to GTR (three trials), we note no statistically significant differences. Clinically, it might be interpreted that BG is equally effective as EMDs and membrane techniques in the treatment of intraosseous defects. BG may end up inducing a "repair" response (formation of long junctional epithelium, new connective-tissue attachment, and ankylosis) rather than a true regenerative response that is characterized by the formation of new periodontal ligament, cementum, and bone. However, when looking at the clinical parameters (PD/CAL), the analysis shows an improvement versus OFD alone. Given that BG products are less expensive than membranes and growth factors, BG may provide a cost-effective method for the treatment of these types of periodontal defects. Although GTR is widely used in clinical practice, it is a technically demanding procedure, and barrier membranes are costly. BG may provide an equally efficacious treatment at a reduced cost. Moreover, the costs of these more conservative treatments remain much less than the expenses of extraction and prosthetic replacement. Viewed from that perspective, even gains of 0.5 to 1 mm in PD and CAL with BG compared to OFD alone do not seem clinically insignificant. In addition, any meta-analysis presents pooled results across a spectrum of different practitioners. Some sites have reported much more significant clinical and statistical changes, whereas other sites have had smaller changes or even negative results.

CONCLUSIONS

Our results demonstrate that BG is efficacious in the repair of periodontal defects because the benefit of BG over control treatment was significant in studies comparing BG to OFD. It is possible that different brands of BG vary in their efficacy in treating intraossesous defects, and this should be explored in a future study.

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