Clinical Evaluation of the Combination of Anorganic Bovine-Derived Hydroxyapatite Matrix/Cell-Binding Peptide (P-15) in Particulate and Hydrogel Form as a Bone Replacement Graft Material in Human Periodontal Osseous Defects: 6-Month Reentry Controlled Clinical Study

Sérgio M. Matos,* Fernando A. Guerra,* Jack Krauser,† Francisco Marques,* Jorge M. Ermida,* and Mariano Sanz‡

Background: This prospective, randomized, controlled clinical trial study compared the clinical outcomes of the biomaterial anorganic bovine-derived hydroxyapatite matrix/cell-binding peptide (ABM/P-15) as a biocompatible hydrogel carrier consisting of carboxymethylcellulose and glycerol or in particulate form when used as a bone replacement graft in the treatment of human periodontal infrabony defects.

Methods: Nineteen patients with advanced chronic periodontitis were recruited. All patients had at least two non-adjacent intrabony osseous defects ≥3 mm after completion of cause-related periodontal therapy. The surgical procedures included access flaps for root instrumentation and filling the defect with ABM/P-15 in hydrogel or particulate form. Reentry access flap surgery was performed at 6 months. Changes in soft and hard tissue outcome measurements between baseline and 6 months were evaluated in all defects.

Results: At 6 months, no significant differences between ABM/P-15 hydrogel and ABM/P-15 particulate were demonstrated for the amount of defect fill (3.10 ± 0.85 mm [75.0%] versus 3.09 ± 1.11 mm [73.7%], respectively) or defect resolution (85.8% versus 81.9%). Changes in soft tissue clinical outcomes did not show significant differences between the treatments.

Conclusion: This trial failed to demonstrate superiority of the novel ABM/P-15 hydrogel therapeutic modality over the standard ABM/P-15 particulate graft in the treatment of intrabony periodontal defects. J Periodontol 2007;78:1855-1863.

KEY WORDS
Hydrogel; hydroxyapatite/therapeutic use; periodontal diseases/therapy; regeneration.

The ultimate goal of periodontal treatment is the regeneration of periodontal tissues lost as a result of periodontal disease. Considerable histologic and clinical evidence has been gathered over the last 2 decades indicating that periodontal regeneration can be achieved in humans. In particular, two clinical approaches have been used routinely with considerable success: bone grafting and guided tissue regeneration with barrier membranes. Two recent systematic reviews summarizing the clinical outcomes following application of specific biomaterials to the treatment of deep intrabony defects indicated that these bone grafts and bone substitutes were significantly more effective than open flap debridement in improving attachment levels and
in reducing probing depths (PDs). However, differences in clinical attachment level (CAL) gains varied greatly with respect to the different biomaterials used; because of this heterogeneity in the results between studies, the investigators were unable to draw conclusions on the use of specific graft biomaterials.3

With the goal of achieving a bioactive mineral matrix, Bhatnagar et al.5 developed a synthetic peptide composed of a defined sequence of 15 amino acids, identical to a potent domain of the cell alfa-1 chain receptor of type I collagen. They used particles of hydroxyapatite of bovine origin as carriers of this peptide. This combination would allow the stimulation of fibroblast adhesion and the formation of three-dimensional colonies of extracellular collagen matrix, with mineralization foci, forming a structure similar to bone; in this way, it would improve the efficacy of conventional replacement grafts in the treatment of intrabony defects.

Based on this concept, the replacement graft anorganic bovine-derived hydroxyapatite matrix (ABM) and cell-binding peptide (P-15) was developed. The anorganic matrix of bovine origin is a natural microporous hydroxyapatite. This type of material showed a positive histologic response when implanted in humans,6-10 and it has adequate porosity, size, and shape for use in the treatment of intrabony periodontal defects.11 Multicenter clinical evaluations12,13 of this replacement graft material demonstrated clinical superiority in intrabony defect fill compared to demineralized freeze-dried bone allograft, open flap debridement, and ABM graft material alone. A 36-month follow-up study14 demonstrated that ABM/P-15 had a beneficial effect on the long-term clinical management of periodontal intrabony defects. Moreover, the evaluation of a human biopsy demonstrated periodontal regeneration in a case treated with ABM/P-15.9

Recently, this product was altered with the intent of improving its clinical handling. This was accomplished by combining the ABM/P-15 particulate graft with a biocompatible hydrogel carrier consisting of carboxymethylcellulose and glycerol. There are no data on the clinical efficacy of this new hydrogel combination in the treatment of intrabony periodontal defects. Therefore, the purpose of this controlled clinical study was to compare the efficacy of standard ABM/P-15 particulate graft material to the new hydrogel ABM/P-15 in the treatment of intrabony periodontal defects and to identify any unusual clinical findings or complications.

MATERIALS AND METHODS

Experimental Design
Two different forms of the bone replacement graft (ABM/P-15) were evaluated for the treatment of intrabony defects in a prospective, randomized, controlled, split-mouth clinical trial. At least two intrabony periodontal defects in each patient were treated randomly by the hydrogel form of the ABM/P-15 graft (experimental group) or the particulate form of the ABM/P-15 graft (control group) (Fig. 1). Patients were followed for 6 months.

Study Population
The patients were selected from those attending the Periodontal Clinic at the University of Coimbra Dental School. They were informed in detail about the objectives and possible risks associated with their participation in the study and were asked to agree to participate in the study by signing an informed consent. The Ethical Committee from the University Hospital of Coimbra, Coimbra, Portugal, approved the study protocol, the patient information sheet, and the informed consent.

Nineteen patients with a diagnosis of moderate to severe chronic periodontitis were entered into the study between January and December 2004. Participation criteria included at least two non-adjacent periodontal intrabony defects with an intraosseous component ≥3 mm and PD ≥6 mm (the defect depth was evaluated clinically and radiographically at screening but had to be confirmed intrasurgically); ≥30 years of age; non-smokers at screening; free of systemic diseases or systemic medication that could interfere with the post-surgical healing process; and no endodontic involvement of study teeth and no mobility superior to grade II. Teeth were excluded when their prognosis was bad (teeth with mobility grade III or presenting fremitus) or if the periodontal defect extended to the furcation.

Materials
The anorganic bone matrix used in this clinical investigation is a totally deproteinated bovine-derived...
natural hydroxyapatite with a microporous structure and a particle size ranging from 250 to 420 μm. This replacement graft material incorporates the 15–amino acid sequence (P-15), which is a synthetic replica of the cell-binding domain of type I collagen, in a proportion of 200 ng P-15 for each gram of ABM. Two different forms of this replacement graft were compared: the experimental formulation where the replacement graft is vehicled in a hydrogel (putty-like form)§ and the control formulation, which is the standard particulate ABM/P-15 replacement graft.¶ The hydrogel formulation is ABM/P-15 suspended in a water-based carrier containing sodium carboxymethylcellulose and glycerol, widely used biocompatible components. Both products are commercially available in the United States and the European Union, were supplied by the manufacturer, and were used per the manufacturer’s instructions.

Presurgical Phase
Prior to surgery, all patients received a thorough periodontal examination, including motivation and instructions in oral hygiene, and multiple sessions of scaling and root planing until reaching acceptable levels of plaque control (plaque index [PI] ≤15%) and inflammation control (bleeding index ≤15%). The baseline examination was carried out 4 to 6 weeks after the completion of this basic periodontal therapy.

Surgical Procedure
The surgical procedure consisted of elevation of full-thickness buccal and lingual mucoperiosteal flaps at the affected teeth. Once the flaps were reflected and the granulation tissue was eliminated completely, the selected defects were debrided meticulously, and the affected roots were scaled and planed with ultrasonic and manual instruments. The intrasurgical measurements were recorded, and the experimental or control replacement grafts were selected randomly. The randomization was done by rolling a die and assigning the odd numbers to ABM/P-15 particulate and the even numbers to ABM/P-15 hydrogel. Because some patients harbored more than two defects, the number of selected defects was not identical for each treatment modality (Fig. 1). Forty-seven defects were treated: 26 with the control replacement graft and 21 with the experimental graft. For consistency in the measurements, the site at each selected defect with the deepest intrabony component was identified and measured, and it was used for the follow-up examinations. The selected replacement graft was packed carefully in the interior of the defect until it was filled completely and level with the alveolar crest. The flaps were repositioned, aiming primary closure without any tension, and sutured. All surgical procedures were performed by two well-trained periodontists (SMM and FAG).

Post-Surgical Instructions and Infection Control
Patients were put on systemic doxycycline for 10 days: 200 mg on the day of surgery and then 100 mg per day for the following 10 days. All patients were instructed to rinse with 0.12% chlorhexidineOffice twice a day for 6 weeks and were not allowed to perform any interden- tal hygiene procedures during this period. Sutures were removed 2 weeks post-surgery.

All patients were placed on a strict recall schedule following surgery (2, 4, and 6 weeks and 3 and 6 months). At every recall appointment, the healing was evaluated and patients were asked about any post-surgical complications. At these visits, a professional supragingival polishing was carried out together with oral hygiene reinforcement. The study concluded at the 6-month visit, when the reentry procedure was scheduled, and then all patients were placed on routine recall. Reentry flap surgeries were performed to visualize the defects under investigation and obtain documentation of the hard tissue outcome measurements.

Outcome Measurements
All clinical recordings were made by a single calibrated examiner (JK), who was not one of the periodontists who performed the regenerative surgical procedures. The evaluator was masked to the treatment provided for each bony defect. Intraexaminer calibration was determined by taking repeated measurements of the same pockets until reaching a high degree of repeatability (90% agreement within 1 mm).

Main outcome measurements: soft tissues. Measurements included CAL measured from the cemento-enamel junction (CEJ) or the restoration margin to the depth of the pocket; PD measured from the gingival margin to the depth of the pocket; and recession measured from the CEJ or the restoration margin to the gingival margin. All measurements were recorded with a pressure-sensitive manual probe immediately prior to the surgery (baseline) and 6 months later.

Secondary outcome measurements. PI according to Turesky et al.15 and modified gingival index (GI) according to Lobene et al.16 were recorded to assess the patient’s hygiene and infection control.

Main outcome measurements: hard tissues. During the regenerative procedure and once the defects were debrided completely, the following intrasurgical measurements were recorded (Fig. 2A): from the CEJ or restoration margin to the alveolar crest (CEJ–AC) and from the CEJ or restoration margin to the bottom of the defect (CEJ–BD). The intrasosseous component of the defect was calculated as (CEJ–BD) – (CEJ–AC).

§ PepGen P-15 Flow, Dentsply CeraMed Dental, Lakewood, CO.
¶ PepGen P-15, Dentsply CeraMed Dental.
† Clorhexidina LACER, Lacer, Barcelona, Spain.
# Vivacare TPS Probe, Vivadent, Schaan, Liechtenstein.
The reentry surgery consisted of elevation of buccal and lingual full-thickness flaps at the affected teeth, removal of all soft tissue in the interproximal area, and evaluation of the hard tissue in the treated defects (Figs. 2B and 2C). By comparing these data with the intrasurgical measurements, we were able to calculate the changes in the bone crest (CEJ–AC between baseline and 6 months), the defect bone fill (CEJ–BD between baseline and 6 months), and the defect resolution (AC–BD between baseline and 6 months).

**Data Analysis**
We considered the split-mouth design as a specialized form of a randomized block design, where the subject serves as the block. Therefore, the subject is the unit of analysis, with the difference between treatments within each subject consisting of the outcome to be analyzed. Based on previous clinical trials using the same bone replacement graft, we designed a study with a similar sample size.

The t test or Wilcoxon signed-rank test for paired data (depending on the normality of the distribution) was used to compare the response between the experimental and control replacement grafts for the soft and hard tissue main outcome variables. Intragroup changes between baseline and 6 months of the same variables also were assessed using the paired t test. The Fisher exact test was used to compare the percentage of predominant walls between groups at baseline. A significance level of 5% was established.

**RESULTS**

**Patient Follow-Up**
All 19 patients (13 males and six females with a mean age of 49 years and ranging in age from 36 to 64 years) completed the study. Twenty-one defects were evaluated in the experimental group (ABM/P-15 hydrogel), and 26 defects were evaluated in the control group (ABM/P-15 particulate); all soft and hard tissue outcome measurements were recorded at baseline and 6 months (Fig. 2). Table 1 shows the characteristics of the study population at baseline. When comparing both treatment groups, no differences were encountered for any of the studied variables.

**Oral Hygiene**
Plaque control and inflammation around the affected teeth did not show any difference between the groups at baseline (Table 1). During the 6 months of the study, both indexes remained stable (between 0.5 and 0.6 for PI and between 0.2 and 0.3 for GI), which

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**Table 1.**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ABM/P-15 Hydrogel</th>
<th>ABM/P-15 Particulate</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (N)</td>
<td>19</td>
<td>19</td>
<td>NS</td>
</tr>
<tr>
<td>PI (mean ± SD)</td>
<td>0.52 ± 0.90</td>
<td>0.66 ± 0.97</td>
<td>NS</td>
</tr>
<tr>
<td>GI (mean ± SD)</td>
<td>0.26 ± 0.45</td>
<td>0.38 ± 0.55</td>
<td>NS</td>
</tr>
<tr>
<td>PD (mm; mean ± SD)</td>
<td>5.92 ± 1.23</td>
<td>6.34 ± 1.66</td>
<td>0.23 (NS)</td>
</tr>
<tr>
<td>CAL (mm; mean ± SD)</td>
<td>7.36 ± 1.74</td>
<td>8.43 ± 2.41</td>
<td>0.08 (NS)</td>
</tr>
<tr>
<td>REC (mm; mean ± SD)</td>
<td>1.44 ± 1.36</td>
<td>2.09 ± 1.68</td>
<td>0.09 (NS)</td>
</tr>
<tr>
<td>INTRA (mm; mean ± SD)</td>
<td>4.12 ± 1.04</td>
<td>4.15 ± 0.91</td>
<td>NS</td>
</tr>
<tr>
<td>Predominantly 1-wall (%)</td>
<td>9.5</td>
<td>15.4</td>
<td>NS</td>
</tr>
<tr>
<td>Predominantly 2-wall (%)</td>
<td>47.6</td>
<td>50.0</td>
<td>NS</td>
</tr>
<tr>
<td>Predominantly 3-wall (%)</td>
<td>42.9</td>
<td>34.6</td>
<td>NS</td>
</tr>
</tbody>
</table>

**REC** = recession; **INTRA** = intraosseous component of the defect; **NS** = not statistically significant (P > 0.05).
demonstrated that the population had a high degree of oral hygiene and inflammation control.

**Main Outcome Measurements**

Postoperative healing was uneventful in all cases and revealed excellent soft tissue response in both treatment groups. There were no untoward effects or patient complaints related to the particulate or hydrogel bone graft substitutes. Upon reentry, the particulate material in the control group (ABM/P-15 particulate) was present on the crestal area of the defect. In the experimental group, the bone crest at the defect site was more homogeneous, although the presence of small particulate material was evident (Figs. 2B and 2C).

Table 2 shows the changes in the hard tissue measurements. The experimental group demonstrated a mean bone fill of $3.10 \pm 0.85$ mm versus $3.09 \pm 1.11$ mm in the control group, which represented a mean defect fill of 75.0% and 73.7%, respectively. Very similar data were obtained for the mean percentages of defect resolution (85.8% ± 10.7% for the experimental group versus 81.9% ± 13.3% for the control group). No significant differences were seen between treatments at 6 months for any of the outcome measurements.

Table 3 shows the changes in the soft tissue measurements. In both groups, gains in CAL were ~3 mm (2.89 ± 1.58 in the experimental group versus 3.41 ± 1.95 in the control group), PD reductions were ~4 mm (4.02 ± 1.19 in the experimental group versus 4.19 ± 1.55 in the control group), and changes in gingival recession were −1.13 ± 0.96 mm in the experimental group and −0.75 ± 1.08 mm in the control group. At 6 months, there were no significant differences between the groups for any of the outcome measurements. A clinical example is shown in Figure 2.

When intragroup differences were evaluated (Table 4), gains in CAL and PD reductions between baseline and 6 months were statistically significant in both groups ($P < 0.0001$). In both groups, gingival recession increased between baseline and 6 months; these differences were significant for both treatment groups, especially the experimental group.

The frequency distribution of the CAL gains is depicted in Table 5. Clinically significant CAL gains (≥4 mm) were obtained in 21.7% of the defects treated with ABM/P-15 in hydrogel versus 46.9% of the defects treated with ABM/P-15 particulate. Table 6 shows the frequency distribution of defect bone fill. The mean percentage of clinically significant defect bone fill (≥80%) was similar with both replacement grafts (39.1% in the experimental group versus 34.4% in the control group).

**DISCUSSION**

This study used a split-mouth design as a specialized form of a randomized block design where the subject is the unit of analysis. This design has been considered adequate for evaluating periodontal regenerative procedures in a recent systematic review evaluating the efficacy of guided tissue regeneration procedures, where half of the selected controlled randomized clinical trials (eight of 16 selected studies) used this split-mouth design. The sample size calculation used in this study was not designed for an equivalence clinical trial because this study aimed to carry out a
Table 4.

Intra- and Intergroup Comparisons (mean ± SD) of Soft Tissue Clinical Parameters Between Baseline and 6 Months

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>6 Months</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAL (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABM/P-15 H</td>
<td>7.36 ± 1.74</td>
<td>4.47 ± 1.13</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ABM/P-15 P</td>
<td>8.43 ± 2.41</td>
<td>5.13 ± 1.61</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean difference</td>
<td>1.07</td>
<td>0.65</td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.08 (NS)</td>
<td>0.09 (NS)</td>
<td></td>
</tr>
<tr>
<td>REC (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABM/P-15 H</td>
<td>1.44 ± 1.36</td>
<td>2.57 ± 1.25</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ABM/P-15 P</td>
<td>2.09 ± 1.68</td>
<td>2.80 ± 1.39</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Mean difference</td>
<td>0.64</td>
<td>0.22</td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.09 (NS)</td>
<td>0.22 (NS)</td>
<td></td>
</tr>
<tr>
<td>PD (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABM/P-15 H</td>
<td>5.92 ± 1.23</td>
<td>1.86 ± 0.94</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ABM/P-15 P</td>
<td>6.34 ± 1.66</td>
<td>2.24 ± 0.70</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean difference</td>
<td>0.42</td>
<td>0.35</td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.23 (NS)</td>
<td>0.08 (NS)</td>
<td></td>
</tr>
</tbody>
</table>

ABM/P-15 H = hydrogel graft; ABM/P-15 P = particulate graft; NS = not statistically significant (P > 0.05); REC = recession.

Table 5.

Frequency Distribution (%) of CAL Gain at 6 Months

<table>
<thead>
<tr>
<th>CAL Gain (mm)</th>
<th>0 to 1</th>
<th>2 to 3</th>
<th>4 to 5</th>
<th>≥6</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABM/P-15 hydrogel</td>
<td>13.1</td>
<td>65.2</td>
<td>13.0</td>
<td>8.7</td>
</tr>
<tr>
<td>ABM/P-15 particulate</td>
<td>15.6</td>
<td>37.5</td>
<td>37.5</td>
<td>9.4</td>
</tr>
</tbody>
</table>

Table 6.

Frequency Distribution (%) of Bone Defect Fill at 6 Months

<table>
<thead>
<tr>
<th>Bone Fill (%)</th>
<th>≤50</th>
<th>&gt;50 to &lt;80</th>
<th>≥80 to &lt;100</th>
<th>100</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABM/P-15 hydrogel</td>
<td>13.1</td>
<td>47.8</td>
<td>21.7</td>
<td>17.4</td>
</tr>
<tr>
<td>ABM/P-15 particulate</td>
<td>12.5</td>
<td>53.1</td>
<td>18.8</td>
<td>15.6</td>
</tr>
</tbody>
</table>

preliminary comparison of the clinical efficacy of a new bone replacement graft with a new presentation for clinical use. However, this sample size is consistent with other clinical trials using xenogenic bone grafts (ranging from 17 to 23 patients); we did not compare the experimental replacement graft to the open flap debridement (negative control) with this sample because many studies already demonstrated the statistical superiority of natural hydroxyapatite bone grafts over access flap surgery. This fact also was documented recently by two systematic reviews on the efficacy of bone replacement grafts in the treatment of intrabony periodontal defects.

This study failed to demonstrate superiority of the experimental replacement graft over the control. Six months after surgery, both treatments resulted in similar improvements in the studied outcome measures (CAL gain, PD reduction, and defect bone fill). The magnitude of the CAL gain (3.41 mm) and defect bone fill (3.09 mm) observed in the control treatment group (ABM/P-15 particulate) was comparable to the best results obtained (ranging from 1.3 to 4.0 mm for CAL gain and from 2.2 to 3.0 mm for bone fill) in recently published studies using bovine-derived xenogenic grafts in the treatment of intrabony defects. These results are clearly comparable to those reported by Yukna et al. using the same material (ABM/P-15 particulate). In this study, we obtained a mean defect bone fill of 73.7% (3.09 mm) compared to 72.3% (2.8 mm) and 72.9% (2.9 mm) reported in those two previous studies. Similarly, in this study we obtained a defect resolution of 81.9% versus 79.9% and 78.4% reported in those studies. These results also are comparable to those obtained in a clinical trial, using the same experimental design (split-mouth, controlled clinical trial with reentry at 6 months), that also evaluated the efficacy of a bovine-derived xenograft in combination with a collagen membrane. The investigators reported a mean defect bone fill of 3.8 mm and a mean alveolar crest resorption of 0.67 mm. Most of the defects in both treatment groups shared a similar morphology (between 85% and 90% were a combination of 2- and 3-wall defects); therefore, we believe that the presence of at least two bony walls also influenced the magnitude of the CAL gains and defect fill obtained in both groups.

The consistency in the results obtained with this replacement graft gives support to its predictable use in the treatment of periodontal intrabony defects. The differences in CAL gain reported in the different studies can be explained by the known prognostic factors in the outcome of any periodontal regenerative surgery, such as the patient’s plaque and infection control, the patient’s smoking status, the surgeon’s variability, and the surgical technique. In this study, we tried to control all of these factors, and under these circumstances, it is more likely that higher CAL gains and a higher percentage of defect bone fill can be obtained.

The magnitude of the obtained results is dependent on the initial depth of the defect, which also may
explain the slight differences in the results among the previous studies. This is probably the case when comparing our results to the study by Sculean et al., in which the initial periodontal defects were significantly deeper than in this study.

The experimental material that we used (ABM/P-15 hydrogel) demonstrated similar outcomes, compared to the control (ABM/P-15 particulate), in soft tissue variables (mean CAL gain of 2.89 mm and mean PD reduction of 4.02 mm) and in hard tissue variables (mean bone defect fill of 3.1 mm [75.0%] and mean defect resolution of 85.8%). The clinical handling of this new form of hydrogel was very good. The material is supplied in prefilled syringes, which facilitates its application because it does not need prehydration. When evaluating the outcomes obtained with this experimental product, the results showed high variability, and there was a tendency not to see significant differences between the groups. The lower crestal resorption and the resulting lower recession in the control group may have been due to a better space-maintaining capacity of the particulate graft that facilitated the preservation of the supracrestal connective tissue and, with this, the regenerative results. However, the limited sample size of the present study did not allow us to clarify whether the different physical properties of the products had any influence on the regenerative results.

In the search for an ideal bone replacement graft in the treatment of periodontal intrabony defects, its physical properties must allow for the stabilization of the initial blood clot; serve as a scaffolding for the invasion of cells with regenerative capacity, together with blood vessels; and allow for the maintenance of space under the flap. Under these principles, because the hydrogel formulation contains less mineral particles per volume and has a wider space in its matrix, it should allow for a greater invasion of adjacent tissues through these spaces. When evaluating the macroscopic outlook during the reentry surgery, the experimental group showed less granular material than the control group; however, this did not translate into a greater defect bone fill or defect resolution. The only available information on the different biologic behaviors of both products in humans comes from a histologic case report, in which the particulate ABM/P-15 graft was compared to the hydrogel form in two fresh extraction sockets filled with both materials. At 13 weeks, the socket filled with the hydrogel form was void of particles and was filled with tissue with histologic characteristics of woven bone. Compared to the socket filled with the particulate form, the hydrogen-filled socket, besides the absence of granules, demonstrated almost twice the amount of vital bone. A comparative study in dogs, although using a different formulation (ABM/P-15 putty), also resulted in significantly greater bone formation in the defects treated with the putty form (49.3%) compared to the particulate form (14.8%). Conversely, a preclinical study performed in cortical bone defects in rabbits demonstrated that the defects treated with the ABM/P-15 particulate graft had a statistically significantly greater regeneration of new bone, with a more mature type, whereas the defects treated with the ABM/P-15 hydrogel had a greater resorption of the particles. Nevertheless, the positive effect of the hydrogel form on bone formation also was established in vitro by comparing different carriers for the ABM/P-15 particles and for the ABM particles without the P-15 sequence. The carboxymethylcellulose hydrogel carrier containing ABM/P-15 enhanced cell adhesion, enhanced osteoblastic activity with increased osteogenic gene expression for alkaline phosphatase and bone morphogenetic proteins, and promoted matrix mineralization. However, in the present study, the possible differences between the two distinct formulations were not detected, probably because of the small sample size. Therefore, more studies are needed to discern whether the hydrogel form is more advantageous than the standard ABM/P-15 bone replacement graft.

CONCLUSIONS

Based on the results from this clinical trial, it can be concluded that ABM/P-15 particulate and ABM/P-15 hydrogel bone replacement grafts resulted in significant improvements in terms of CAL gain, PD reduction, and bone defect fill compared to baseline. This study failed to demonstrate the superiority of one form of the graft material over the other.

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REFERENCES


Correspondence: Dr. Sérgio Matos, Department of Dental Medicine, Stomatology, and Maxillofacial Surgery, Faculty of Medicine, University of Coimbra, 3000-075 Coimbra, Portugal. Fax: 351-239-402910; e-mail: sergiomatos1@sapo.pt.

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