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Porcine-derived soft block bone substitutes for the treatment of severe class II furcation-involved mandibular molars: a prospective controlled follow-up study

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

ABSTRACT

Purpose: No evidence exists regarding the advantages of periodontal regeneration treatment for furcation defects using soft block bone substitutes. Therefore, this randomized controlled trial aimed to assess the clinical and radiographic outcomes of regenerative therapy using porcine-derived soft block bone substitutes (DPBM-C, test group) compared with porcine-derived particulate bone substitutes (DPBM, control group) for the treatment of severe class II furcation defects in the mandibular molar regions.
Methods: Thirty-five enrolled patients (test group, n=17; control group, n=18) were available for a 12-month follow-up assessment. Clinical (probing pocket depth [PPD] and clinical attachment level [CAL]) and radiographic (vertical furcation defect; VFD) parameters were evaluated at baseline and 6 and 12 months after regenerative treatment. Early postoperative discomfort (severity and duration of pain and swelling) and wound healing outcomes (dehiscence, suppuration, abscess formation, and swelling) were also assessed 2 weeks after surgery.
Results: For both treatment modalities, significant improvements in PPD, CAL, and VFD were found in the test group (PPD reduction of 4.1±3.0 mm, CAL gain of 4.4±2.9 mm, and VFD reduction of 4.1±2.5 mm) and control group (PPD reduction of 2.7±2.0 mm, CAL gain of 2.0±2.8 mm, and VFD reduction of 2.4±2.5 mm) 12 months after the regenerative treatment of furcation defects (P<0.05). However, no statistically significant differences were found in any of the measured clinical and radiographic parameters, and no significant differences were observed in any early postoperative discomfort and wound healing outcomes between the 2 groups.
Conclusions: Similar to DPBM, DPBM-C showed favorable clinical and radiographic outcomes for periodontal regeneration of severe class II furcation defects in a 12-month follow-up period.

Trial Registration: Clinical Research Information Service Identifier: KCT0007305

Keywords: Bone regeneration; Furcation defects; Periodontal diseases; Randomized controlled trial

Author Contributions

Conceptualization: Ji-Hoo Han, Jae-Hong Lee, Seong-Nyum Jeong. Formal analysis: Ji-Hoo Han, Jae-Hong Lee, Seong-Nyum Jeong. Investigation: Ji-Hoo Han, Jae-Hong Lee, Seong-Nyum Jeong. Methodology: Ji-Hoo Han, Jae-Hong Lee, Seong-Nyum Jeong. Project administration: Ji-Hoo Han, Jae-Hong Lee, Seong-Nyum Jeong. Writing - original draft: Ji-Hoo Han, Jae-Hong Lee, Seong-Nyum Jeong. Writing - review & editing: Ji-Hoo Han, Jae-Hong Lee, Seong-Nyum Jeong.

INTRODUCTION

Furcation involvement or defect is defined as periodontally induced pathologic alveolar bone resorption and attachment loss into the bifurcation or trifurcation of a multi-rooted tooth [1]. Over the past several decades, guided tissue regeneration (GTR) with non-resorbable membranes has been usefully and validly applied to furcation defects, and some clinical studies have reported achieving resolution in more than 90% of defects [2,3]. However, owing to the possibility of critical postoperative complications, such as membrane exposure, dehiscence, and severe infection, routine clinical use of the GTR technique is currently limited [4,5].

A recent systematic review concluded that GTR in combination with resorbable collagen membranes and bone grafts for the treatment of class II furcation defects provides additional advantages in terms of defect filling and defect volume reduction, compared to conventional GTR or open flap debridement (OFD) [6]. Deproteinized bovine bone mineral (DBBM), a bone graft material and the first animal bone employed to produce xenografts, has been widely and successfully used in periodontal regenerative treatment, especially for class II furcation defects [7,8]. In more recently developed xenografts, deproteinized porcine bone mineral (DPBM) has also been commonly used in the field of dental materials for clinical applications [9,10]. Several prospective and retrospective studies have demonstrated that DPBM significantly improved clinical and radiographic outcomes following periodontal regeneration treatment [11-13].

Various nonsurgical and surgical treatment techniques, including scaling and root planning, OFD with or without bone graft materials, GTR, and root resection or tunneling, have been devised. However, the ideal materials or treatment modalities for the regenerative treatment of furcation defects remain a matter of debate, and no standard guidelines have been established [1,14]. In addition, several preclinical and clinical studies on bone grafts have reported that more recently devised soft block bone substitutes improved morphological stability and maintenance capacity compared to particulate bone substitutes. However, to the best of our knowledge, no research has focused on the practical benefits of using soft block bone substitutes for periodontal regeneration in cases of furcation defects. Therefore, this prospective randomized clinical trial aimed to determine the clinical and radiographic advantages of using collagenated soft-type DPBM block bone substitutes (DPBM-C) for the periodontal regenerative treatment of severe class II furcation defects in the mandibular molar region.

MATERIALS AND METHODS

Study design

This prospective randomized controlled follow-up study included patients attending the Department of Periodontology at Daejeon Dental Hospital, Wonkwang University, between November 2020 and April 2022. The study protocol was approved by the local Institutional Review Board of Daejeon Dental Hospital, Wonkwang University (approval No. W2011/003-001) and registered with the Republic of Korea Clinical Trials Registry (identifier number: KCT0007305). The study was performed with informed consent and followed the revised Declaration of Helsinki [15]. The Consolidated Standards of Reporting Trial checklist was used to evaluate the reporting quality of the current trial.

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Study population

Patients with furcation involvement were included in this study. The detailed inclusion criteria were as follows: 1) presence of class II (≥3 mm horizontal alveolar bone loss but not through and through) and grade III (≥7 mm vertical probing depth) furcation defect at the buccal aspect of the mandibular first or second molar; 2) age ≥20 years; 3) non-, former, or light (<10 cigarettes/day) smoking; 4) well-controlled or stable periodontal status (<25% full-mouth bleeding score on probing and full-mouth plaque score); and 5) healthy or minimal systemic illness that would not contraindicate a surgical procedure [16,17]. The exclusion criteria were as follows: 1) heavy smoking (≥10 cigarettes/day); 2) uncontrolled or poor periodontal status; 3) uncontrolled systemic disease including diabetes mellitus and hypertension; 4) alcoholism or drug abuse; 5) lactation or pregnancy; and 6) failure to sign an informed consent form.

Procedures and interventions

The surgical procedure was performed by an experienced periodontal specialist (JHL). A sulcular full-thickness mucoperiosteal flap was minimally but sufficiently elevated to expose class II and grade III furcation defects of the mandibular first or second molar under local anesthesia (2% lidocaine HCl with 1:100,000 epinephrine; Yuhan, Seoul, Korea). All plaque, calculus, and granulation tissues were removed with curettes (standard and mini-Gracey curettes; Hu-Friedy, Chicago, IL, USA) and an ultrasonic device (SONICflex air scaler; KaVo, Biberach, Germany). After root conditioning with tetracycline HCl for 2 minutes, enamel matrix derivative (EMD) (Emdogain 0.3 mL; Straumann, Basel, Switzerland) was applied to the debrided and dried root surface. The bone graft materials were then filled in the furcation defect area as follows:

- Test group: After soaking in sterile saline solution for 30 seconds, DPBM-C (DPBM with 10% collagen, THE Graft Collagen 0.34 mL/0.15 g; Purgo Biologics, Seongnam, Korea) was directly and appropriately trimmed according to the shape and size of the furcation defects using a #15 blade. DPBM-C was then filled into the furcation defects using a stainless steel amalgam plugger.
- Control group: DPBM (THE Graft 0.25 g; Purgo Biologics) was filled into the furcation defect.

The flap was repositioned and stabilized using a 4–0 non-absorbable polytetrafluoroethylene monofilament (Biotex; Purgo Biologics) with interrupted and sling sutures. Patients were provided postoperative medication (amoxicillin [500 mg] and ibuprofen [200 mg], 3 times daily for 5 days) and mouthwash (0.12% chlorhexidine digluconate, twice daily for 2 weeks). After 2 weeks, the sutures were carefully removed, and follow-up examinations were performed at 6-month intervals.

Outcome measurements

The observed clinical and radiographic outcomes were measured before surgery (T0), 2 weeks after surgery (T1), at a 6-month follow-up (T2), and at a 12-month follow-up (T3). All measurements were performed by 1 calibrated examiner (JHL), and the intra-rater reliability and reproducibility were high, with intraclass correlation coefficients of over 0.80.

Clinical and radiographic measures

Clinical parameters, including probing pocket depth (PPD) and clinical attachment level (CAL), were measured for each tooth using a periodontal probe (CP 15 UNC periodontal probe; Hu-Friedy) at T0, T2, and T3. Vertical furcation depth (VFD) was measured as the

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distance between the fornix of the furcation and the most apical extension of the furcation defect on periapical radiographs using medical imaging measurement software (OsiriX version 11.0; Pixmeo SARL, Geneva, Switzerland) at T0, T2, and T3.

Early postoperative discomfort and wound healing measures

Early and subjective postoperative discomfort, including severity and duration of pain and swelling, was measured using a visual analog scale score (0–10; 0: no pain and swelling, 10: worst pain and swelling) using a self-reported questionnaire at T1 [18]. Early postoperative wound healing outcomes, including dehiscence, suppuration, abscess formation, and swelling, were also assessed at T1 [19].

Sample size estimation

No previous data on clinical and radiographic outcomes of periodontal regenerative treatment with soft block bone substitutes are available in the literature. Therefore, a sample size calculation was performed to compare a significant difference of 1.0 mm in the bone level between the 2 treatment procedures based on previous studies of OFD with adjunctive use of particulate bone substitutes and EMD [20]. According to a power analysis using statistical power analyses software (G*Power software version 3.1; Franz Faul, Christian-Albrechts-Universität Kiel, Kiel, Germany), a required sample of 17 patients for each group was sufficient to obtain a power of 0.80 and an alpha of 0.05. Allowing for a dropout rate of 20%, 40 patients were required for enrollment.

Randomization and allocation

All enrolled patients were randomly assigned (1:1) to the test (n=20) and control (n=20) groups using a computer-generated table to receive 1 of the 2 treatment methods using permuted blocks of 2 and 4 patients. Randomization and allocation procedures were performed by an assistant who was not involved in the current study.

Statistical analysis

All included categorical and continuous variables are expressed as frequencies (n), proportions (%), means, median, first and third quartiles, standard deviations, and 95% confidence intervals (CIs). The Shapiro-Wilk test was used for data normality verification, and the χ^2 test, independent *t*-test, and paired *t*-test were conducted to determine the significance of differences in clinical, radiographic, and postoperative discomfort and early wound healing outcomes. All statistical analyses were performed using a statistical software program (SPSS version 28.01.0; IBM Corporation, Armonk, NY, USA), and a value of $P<0.05$ was considered to indicate statistical significance.

RESULTS

Forty patients were screened and randomly assigned at a 1:1 allocation ratio to the test and control groups at T0. Of the 35 patients finally included, based on the inclusion and exclusion criteria, 17 (mean age 57.9±8.1 years; 7 men and 10 women) were in the test group and 18 (mean age 51.6±15.9 years; 9 men and 9 women) were in the control group. No statistically significant differences were observed in the baseline characteristics between the 2 groups. The detailed baseline characteristics and flowchart of the participants are presented in **Table 1** and **Figure 1**.

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Table 1. Baseline characteristics of the enrolled patients

Variables	Test group (n=17)	Control group (n=18)	*P*
Sex			0.605
Male	7 (41.2)	9 (50.0)	
Female	10 (58.8)	9 (50.0)	
Age (yr)	57.9±8.1	51.6±15.9	0.217
Smoking habits			0.515
Non-smoker	12 (70.6)	14 (77.8)	
Former smoker	3 (17.6)	1 (5.6)	
Smoker (<10 cigarettes/day)	2 (11.8)	3 (16.7)	
Diabetes mellitus			0.586
Yes	1 (5.9)	2 (11.1)	
Location			0.482
Mandibular first molar	14 (82.4)	13 (72.2)	
Mandibular second molar	3 (17.6)	5 (27.8)	
Periodontal status			
BOP	16 (94.1)	18 (100.0)	0.303
GI	2.2±0.6	2.3±0.5	0.641
PI	1.8±0.7	1.7±0.8	0.736

Values are presented as mean ± standard deviation or number (%).
BOP: bleeding on probing, GI: gingival index, PI: plaque index.

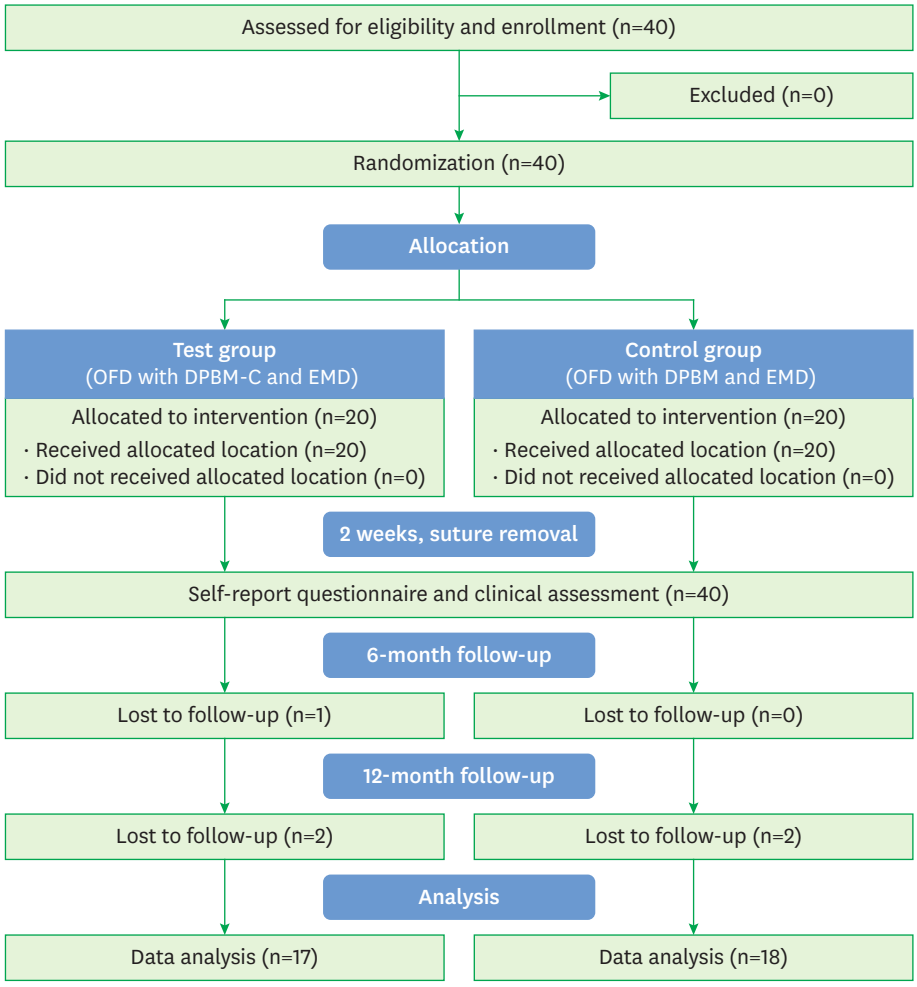

Figure 1. Flow chart for study patients.
OFD: open flap debridement, EMD: enamel matrix derivative, DPBM: demineralized porcine bone matrix, DPBM-C: deproteinized porcine bone mineral with 10% collagen.

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Clinical and radiographic outcomes

Table 2 presents the clinical and radiographic measurements at T0, T2, and T3. Twelve months after the regenerative treatment of severe class II furcation defects, significant improvements in PPD, CAL, and VFD were observed in the test and control groups (P<0.05). At T2, the test group showed significant changes in PPD, CAL, and VFD, from 9.3±1.9 mm to 5.2±2.2 mm (P<0.001), 10.0±1.5 mm to 5.8±2.0 mm (P<0.001), and 6.4±1.2 mm to 2.5±2.0 mm (P<0.001), respectively, while the control group showed significant changes in PPD, CAL, and VFD, from 8.2±1.6 mm to 5.9±2.4 mm (P=0.010), 8.8±1.3 mm to 6.6±2.3 mm (P=0.008), and 5.1±1.7 mm to 2.9±1.9 mm (P=0.007), respectively. In both groups, the clinical and radiographic improvements observed at T2 were sustained until T3 (P>0.05). No statistically significant differences between the test and control groups were found in clinical and radiographic outcomes after treatment for severe class II furcation defects at T0, T2, and T3, respectively (**Figure 2**).

Early postoperative discomfort and wound healing outcomes

The severity of pain (test group: 4.1±2.2, control group: 3.8±1.7, P=0.694) and swelling (test group: 4.8±1.9, control group: 4.2±1.8, P=0.433) and the duration of pain (test group: 4.6±2.6, control group: 4.7±2.7, P=0.920) and swelling (test group: 4.3±2.7, control group: 4.2±3.7, P=0.988) did not differ significantly between the 2 compared groups (**Figure 3A**). In the test group, dehiscence, suppuration, abscess, and swelling occurred in 4 (23.5%), 1 (5.9%), 1 (5.9%), and 3 (17.6%) patients, respectively. In the control group, dehiscence, suppuration, abscess, and swelling occurred in 3 (16.7%), 1 (5.6%), 1 (5.6%), and 2 (11.1%) patients, respectively. No statistically significant differences were observed in any wound healing complications between the 2 groups (**Figure 3B**).

Table 2. Clinical and radiographic outcomes at furcation defects

Parameters (mm)	Test group					Control group				
	Baseline (T0)	6 mo follow-up (T2)	P^a	12 mo follow-up (T3)	P^b	Baseline (T0)	6 mo follow-up (T2)	P^a	12 mo follow-up (T3)	P^b
PPD	9.3±1.9 (9.1 [7.9, 9.4])	5.2±2.2 (4.6 [3.5, 6.4])	<0.001	5.1±2.8 (4.1 [3.1, 6.8])	0.967	8.2±1.6 (7.9 [7.2, 8.6])	5.9±2.4 (6.2 [3.6, 7.6])	0.010	5.6±2.2 (4.7 [4.3, 5.6])	0.692
CAL	10.0±1.5 (9.6 [9.3, 10.6])	5.8±2.0 (5.3 [4.5, 6.2])	<0.001	5.6±2.2 (4.5 [4.4, 5.4])	0.810	8.8±1.3 (8.7 [8.2, 9.4])	6.6±2.3 (6.8 [4.3, 7.9])	0.008	6.9±2.3 (6.0 [5.6, 6.7])	0.786
VFD	6.4±1.2 (6.5 [5.6, 7.0])	2.5±2.0 (1.8 [1.7, 2.2])	<0.001	2.3±2.0 (1.9 [0.9, 3.3])	0.788	5.1±1.7 (4.9 [4.1, 5.2])	2.9±1.9 (2.4 [1.5, 3.9])	0.007	2.7±1.8 (2.3 [1.7, 3.1])	0.713

Data are expressed as mean ± standard deviation (median [first and third quartiles]), and boldface denotes statistical significance (P<0.05).
PPD: probing pocket depth, CAL: clinical attachment level, VFD: vertical furcation depth.
P-values for comparisons between [a]T0 versus T2 and [b]T2 versus T3.

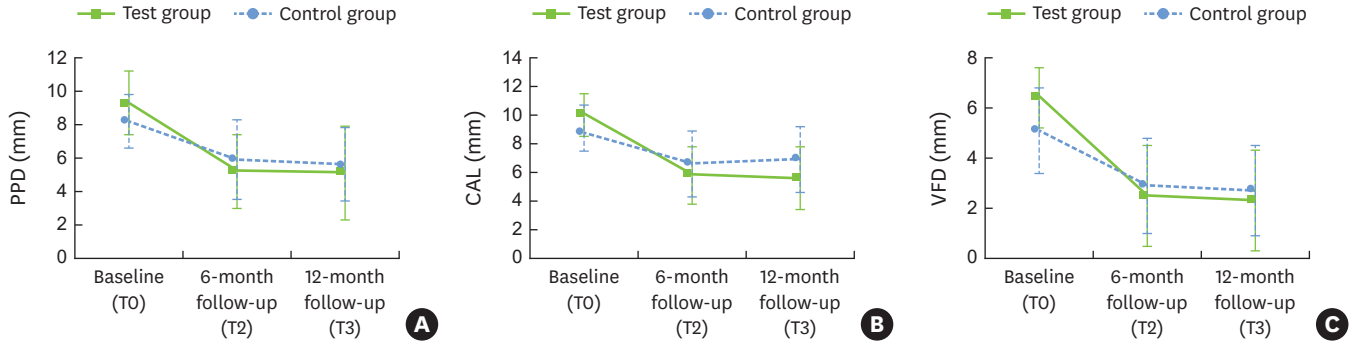

Figure 2. Comparison of clinical and radiographic outcomes between the test and control groups after treatment for severe class II furcation defects. (A, B) Clinical outcomes at T0, T2, and T3, measured as PPD and CAL. (C) Radiographic outcomes at T0, T2, and T3, measured as VFD.
PPD: probing pocket depth, CAL: clinical attachment level, VFD: vertical furcation depth.

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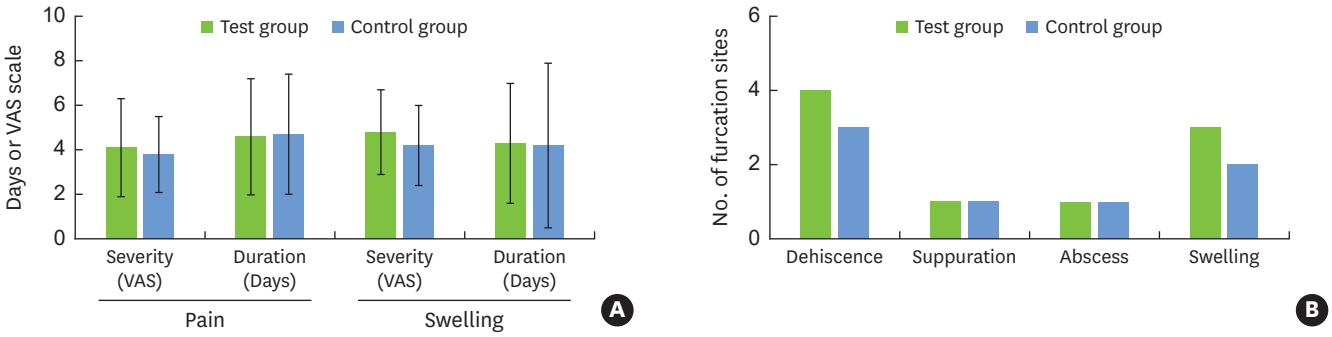

Figure 3. Comparison between the test and control groups of early postoperative discomfort and wound healing outcomes. (A) Severity and duration of pain and swelling. (B) Clinical assessment of soft tissue early wound healing outcomes during suture removal.
VAS: visual analogue scale.

DISCUSSION

Although OFD alone can generate new attachments and bone formation in the treatment of furcation defects, additional applications of various biomaterials are being attempted to achieve greater clinical benefits of regenerative procedures in the treatment of severe types of furcation defects [21]. Nevertheless, the successful treatment of furcation defects has been considered one of the most difficult and challenging clinical problems because of the inadequate visual field and instrument access due to the complex anatomy and varying morphologies [22].

GTR is one of the best-documented periodontal regeneration procedures and has been effectively and predictably used for clinical and histological improvements [23]. When limited to mandibular class II furcation defects, a systematic review reported that GTR further reduced the horizontal furcation depth by 1.51 mm (95% CI, 0.39–2.62) on average compared to conventional OFD (P<0.001), and another more recent systematic review also confirmed that GTR provided significantly superior outcomes of 1 mm or more on average in terms of horizontal and vertical defect reduction and bone fill compared to OFD [24,25]. However, because GTR is technically sensitive and has the potential to expose non-resorbable and resorbable membranes, there remains a clinical burden [5,26].

Various studies have reported the clinical and radiological outcomes of the adjunctive use of EMD for class II or class III furcation defects [27-29]. One clinical study reported that the adjunctive use of EMD significantly enhanced the horizontal and vertical resolution of the mandibular class II furcation defects (P<0.05) [27]. Another histological study suggested that GTR in combination with EMD for mandibular class III furcation defects had a higher probability of periodontal regeneration, including new attachment and new bone formation, than OFD alone [28]. Similarly, a long-term randomized clinical trial that compared patients with and without the adjunctive use of EMD reported that OFD with EMD significantly reduced PPD and the number of furcation defects (P<0.05) [29]. However, a recent systematic review and meta-analysis demonstrated that the evidence base for clinical benefits of the adjunctive use of EMD in the treatment of class II furcation defects was still insufficient and emphasized the need to address this issue through more large-scale studies [30].

In addition, the results of animal and human studies related to the use of bone grafts in combination with EMD are still limited and inconsistent [31]. A histological and histometric

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study showed that the adjunctive use of EMD with bone graft did not have a statistically significant positive effect on the results of periodontal regeneration treatment of class III furcation defects in dogs [32]. Conversely, another clinical study conducted in mandibular class II furcation defects reported that the adjunctive use of a bone graft with EMD resulted in a statistically significant reduction in PPD and gain in vertical relative attachment level, and a non-significantly greater reduction in horizontal PPD than achieved with a bone graft alone [33]. However, since most of the pre-clinical and clinical studies related to bone grafting with EMD were limited to intrabony defects, there is a very limited degree to which the findings of this study can be directly compared with others in the literature.

To the best of our knowledge, this prospective study is the first to evaluate the clinical and radiographic outcomes of severe class II furcation defects in the mandibular molar region after periodontal regenerative treatment with DPBM-C. Although the results of this study indicate that OFD with DPBM-C in combination with EMD can be considered useful for resolving furcation defects, no additional clinical and radiological advantages could be found compared with OFD with DPBM and EMD. However, despite the absence of statistical significance, all clinical and radiographic outcomes, including PPD, CAL, and VFD, improved in the test group compared with the control group. In addition, considering the early postoperative discomfort and wound healing outcomes, the results of the test group were not inferior to those of the control group, and these results indicate that DPBM-C can be applied favorably to severe furcation defects. In the test and control groups, which showed early postoperative inflammation (including dehiscence, suppuration, abscess formation, and swelling), antibiotics and mouthwash were additionally prescribed, and active patient follow-up was performed twice a week. All inflammatory furcation defects subsided adequately within 3 weeks without critical complications and were therefore included in the clinical and radiological analyses of this study. In addition, smoking is a major risk factor for a poor prognosis of periodontal defects; nonetheless, smokers who smoked fewer than 10 cigarettes per day were included in this study. However, due to the small number of light smokers included, we could not identify a statistically significant difference in the early postoperative discomfort and wound healing outcomes between smokers and non-smokers in the test and control groups.

For small defects, it is difficult to trim the block bone properly or fit it into the furcation defect. Therefore, only severe and deep furcation defects were included to evaluate the clinical and radiographic benefits of soft block bone substitutes. In this study, some clinical characteristics or benefits of soft block bone substitutes were observed. First, soft block bone substitutes are more advantageous than particulate bone substitutes in terms of space maintenance and mechanical support properties for severe furcation defects. However, volumetric and profilometric analyses should be performed to confirm these advantages clearly and directly. In addition, proper manipulation and easy trimming according to the shape of the furcation defect morphology are other advantages of soft block bone substitutes.

Although this study convincingly presents fact-based evidence, it has some limitations. The major limitation of the current study was that we did not design a negative control group without bone grafting in combination with EMD, which could be used to directly compare the results of periodontal regeneration treatment. Second, the follow-up period may not have been sufficient to confirm the overall clinical and radiographic outcomes and the efficacy of periodontal treatment interventions for severe class II furcation defects. Third, because calibrated periodontal probes or individual acrylic resin occlusal stents were not

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used in this study, caution is needed when interpreting the measurement reproducibility. Another limitation is that volumetric, profilometric, histological, and histomorphometric analyses were not performed to confirm the additional clinical advantages of soft block bone substitutes. Therefore, further long-term and well-designed randomized controlled clinical trials to treat furcation defects are necessary to confirm these findings.

In conclusion, within the limitations of this study, periodontal regenerative treatment with DPBM-C showed improved clinical and radiographic outcomes for severe mandibular class II furcation defects in a 12-month follow-up period. In addition, no significant differences were observed in any clinical, radiographic, or early postoperative discomfort and wound healing outcomes between the DPBM-C and DPBM groups.

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