Evaluation of the Effectiveness of Enamel Matrix Derivative, Bone Grafts, and Membrane in the Treatment of Mandibular Class II Furcation Defects

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The combination of osseous graft with barrier membrane and enamel matrix protein derivative (EMD) has the potential to result in a synergistic effect. Therefore, the aim of this study was to evaluate the effectiveness of EMD in combination with demineralized freeze-dried bone allograft (BG) and bioresorbable membrane (Biomesh) in the treatment of human mandibular Class II furcation defects over a period of 12 months. Thirty patients with chronic periodontitis and a single Class II furcation defect on the buccal or lingual surface of mandibular teeth were included. The clinical parameters evaluated were probing pocket depth (PPD), horizontal probing depth (HPD), vertical relative attachment level (V-RAL), and relative gingival margin level (RGML). three groups were created based on treatment method: EMD + BG + guided tissue regeneration (GTR), BG + GTR, and open flap debridement (OFD). All three groups showed a statistically significant PPD reduction of 1.74 ± 1.00 mm, 0.81 ± 0.31 mm, and 0.46 ± 0.52 mm at 12 months postsurgery. EMD + BG + GTR showed a significantly greater PPD reduction compared with BG + GTR, as well as OFD. EMD + BG + GTR showed a statistically significant vertical clinical attachment gain of 2.12 ± 1.07 mm at 12 months compared with BG + GTR as well as OFD. Significant reductions in mean HPD were observed for EMD + BG + GTR (2.10 mm) as well as BG + GTR (1.5 mm). The number of Class II furcation defects that closed or converted to Class I was greatest for EMD + BG + GTR. It can be concluded that EMD + BG + GTR resulted in a statistically significant reduction of PPD, V-RAL gain, and a nonsignificantly greater reduction of HPD compared to BG + GTR. (Int J Periodontics Restorative Dent 2013;33:e58–e64. doi: 10.11607/prd.1428)

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One of the greatest challenges in periodontics continues to be the treatment of multirooted teeth demonstrating interradicular loss of periodontal tissues.[1–4] A Class II furcation defect indicates a common clinical problem and a need for effective therapy.[5–7]

Several comparative studies using bioresorbable and nonabsorbable barriers for guided tissue regeneration (GTR) therapy for furcation defects have been performed. While some reports demonstrated a significant attachment gain, other studies did not show significant clinical improvement.[8,9] It has been suggested that the combination of bone graft (BG) with GTR membrane would provide the most beneficial regenerative therapy for Class II furcations[10]; however, results obtained in clinical controlled studies have demonstrated that the use of BG together with barrier membrane was of limited significance in providing an additional benefit over a membrane alone.[7,11]

Enamel matrix protein derivative (EMD) may represent a potentially valuable component for periodontal regeneration. Multiple clinical studies and case reports have provided evidence for the ability of EMD to promote increased bone and attachment level gains in periodontal defects.[12–15] A combination of BG with barrier membrane and EMD has the potential to result in a synergistic effect, where the BG acts as a scaffold for maintaining the dead space, selective repopulation of the periodontal wound occurs by interposing a barrier membrane, and EMD works at the root level by promoting periodontal regeneration. Therefore, this randomized, controlled, parallel design study was undertaken to evaluate the effectiveness of EMD in combination with demineralized freeze-dried bone allograft (BG) and bioresorbable membrane (Biomesh) in the treatment of human mandibular Class II furcation defects.

Method and materials

A total of 30 systemically healthy patients with chronic periodontitis (mean age, 36.6 ± 1.3 years) were selected from the Department of Periodontics, S.P. Dental College, Wardha, India. The patients were required to fulfil the following inclusion criteria: *(1)* the presence of a Class II furcation defect on buccal/lingual surfaces of mandibular molars as determined by clinical and radiographic evaluation, *(2)* the presence of ≥ 3 mm horizontal furcation probing depth not entirely through the furcation,[16] and *(3)* gingival margin positioned coronal to the furcation fornix. Patients with unacceptable oral hygiene (plaque score > 1),[17] smokers, and pregnant women or lactating mothers were excluded from the study.

After proper examination and diagnosis, oral hygiene instructions were delivered and supra- and subgingival scaling and root planing were performed. Coronoplasty was performed, if necessary. Plaque control instructions were repeated until the patient achieved a plaque score of ≤ 1.

Clinical measurements

On the day of the surgical procedure, a full-mouth score was assessed using the Plaque Index (PI).[17] Gingival inflammation was assessed using the Papillary Bleeding Index (PBI).[18] Measurements recorded for assessment of results were vertical probing pocket depth (PPD), horizontal probing depth (HPD), vertical relative attachment level (V-RAL), and relative gingival margin level (RGML). The measurements were recorded at three sites of each furcation surface for each tooth: the mesial line angle, distal line angle, and midbuccal/midlingual. For later calculations, the mean of the three sites was taken into consideration. These measurements, except HPD, were recorded with a computerized, constant-force probe (Florida Disk Probe, Florida Probe) (Fig 1). HPD was recorded using a curved furcation probe (Naber's probe PQ2N, Hu-Friedy). The operator recorded all measurements at baseline and at 6 and 12 months postsurgery. Complete closure of the defect was assessed at the end of the 12-month period using the bone sounding procedure.

The surgical procedure included a presurgical rinse, administration of local anesthesia (2% xylocaine with 1:100,000 adrenaline), and a raised full-thickness mucoperiosteal flap on both the facial and lingual surfaces. Granulation tissue in the furcation defect was removed, and the exposed root surface, including the roof of the furcation, was scaled and planed using hand and ultrasonic instruments. The defects were measured at their deepest point both vertically and horizontally after flap elevation and debridement (Fig 2). After assessment of the intrasurgical parameters, the sites were randomly assigned to one of three groups using computer software (RAS): EMD + BG + GTR, BG + GTR, or open flap debridement (OFD) (EMD, Emdogain, Biora; BG-MTF; demineralized freeze-dried bone allograft; GTR: BioMesh-S, Samyang).

Surgical procedure

BG was combined with EMD to create a putty-like material that was condensed into the furcation defect (Fig 3). EMD was also applied to the root surface and the furcation defect (Fig 4). GTR membrane was secured over the furcation defect using sling sutures (Fig 5). Finally, the flap was repositioned to completely cover the membrane and sutured with 4-0/5-0 Mersilk sutures (Ethicon,

Fig 1 *Baseline defect measurement using a Florida Disk Probe.*

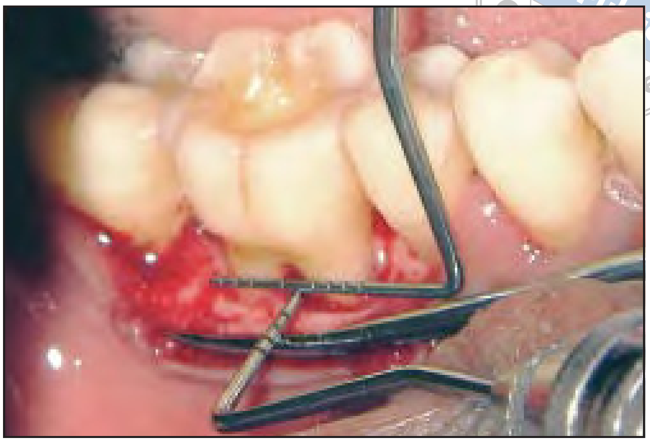

Fig 2 *Intraoperative defect measurement.*

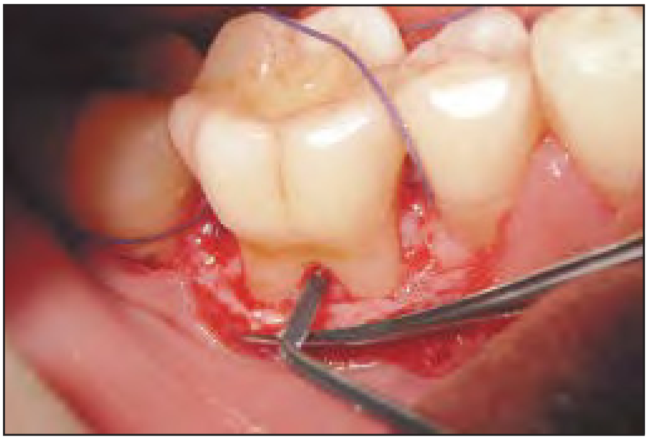

Fig 3 *EMD applied at the root surface and site of defect.*

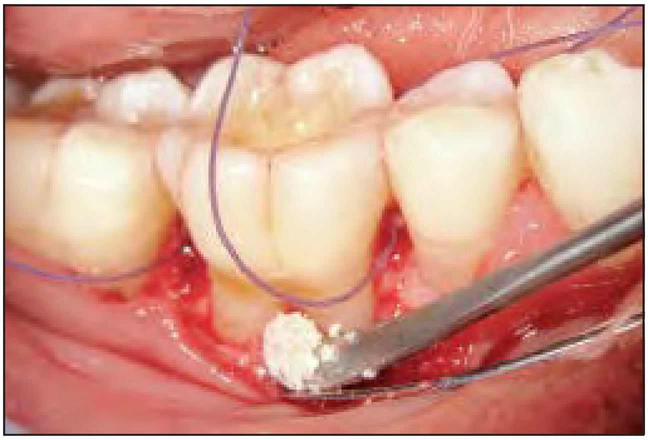

Fig 4 *Bone graft placed in defect.*

Fig 5 *Placement of GTR membrane.*

Johnson & Johnson) using the vertical mattress or interrupted suturing technique. The surgical procedure for BG + GTR was similar to that for EMD + BG + GTR except for the application of EMD. The control group (OFD) did not receive any GTR membrane, BG, or EMD.

After surgery, patients were prescribed a nonsteroidal anti-inflammatory medication (Ibugesic plus [ibuprofen + paracetamol],

Table 1 Intrasurgical hard tissue measurements at baseline (mean ± SD)

Parameters	OFD	EMD + BG + GTR	Difference	BG + GTR	Difference
Horizontal defect depth (mm)	4.50 ± 0.97	3.9 ± 0.56	0.40 ± 0.35 (*P* = .27)	4.10 ± 0.56	0.40 ± 0.35 (*P* = .27)
Vertical defect depth (fornix to base of defect, mm)	4.50 ± 1.71	3.70 ± 0.82	0.60 ± 0.59 (*P* = .32)	3.90 ± 0.73	0.60 ± 0.59 (*P* = .32)

SD = standard deviation; OFD = open flap debridement; EMD = enamel matrix protein derivative; BG = bone graft; GTR = guided tissue regeneration.

tds for 5 days) and systemic antibiotics (amoxicillin, 500 mg, tds for 7 days). Patients were placed on 0.2% chlorhexidine gluconate twice daily for 4 to 6 weeks. Patients were instructed to avoid undue trauma to the treated site. Clinical measurements recorded preoperatively were repeated at 6 and 12 months postsurgery.

Results

The mean PI and PBI scores at baseline and at 6- and 12-months follow-up remained low (< 1). At baseline, none of the investigated parameters showed a significant difference between all three groups ($P > .05$), indicating that the randomization process was effective (Table 1).

For OFD, the mean PPD decreased nonsignificantly ($P > .05$) from baseline to 6 months. However, at 12 months, the reduction in PPD was statistically significant. A Student paired *t* test indicated that the mean PPD reductions for BG + GTR and EMD + BG + GTR at 6 and 12 months were statistically significant ($P < .05$) (Table 2). When 12-month individual data for mean PPD reduction for EMD + BG + GTR and BG + GTR were compared with OFD, mean reductions were found to be significantly greater. There was a significantly greater PPD reduction (0.83 ± 0.29 mm) noted for EMD + BG + GTR compared with the BG + GTR (Table 3).

Student paired *t* test indicated that the mean gain in V-RAL for OFD at 6 and 12 months was statistically nonsignificant. Similarly, for BG + GTR and EMD + BG + GTR, the mean V-RAL gain was statistically significant (Table 2). When individual comparisons were made of clinical attachment gain for EMD + BG + GTR (2.12 ± 1.07 mm) and BG + GTR (0.85 ± 0.31 mm) with that for OFD (0.34 ± 0.74 mm) at 12 months, the difference was found to be statistically significant for EMD + BG + GTR and nonsignificant for BG + GTR. At 12 months, there was a greater and statistically significant mean attachment level gain of 1.27 ± 0.35 mm for EMD + BG + GTR compared with BG + GTR (Table 3).

The mean difference in RGML observed at 6 and 12 months was statistically nonsignificant for all treatment methods (Table 2).

The mean HPD for OFD decreased from 4.50 ± 1.71 mm at baseline to 4.20 ± 1.54 mm at 6 months and 4.00 ± 1.24 mm at 12 months. The mean reduction in HPD observed at 6 and 12 months was statistically nonsignificant. However, for BG + GTR and for EMD + BG + GTR, the mean reduction in HPD at 6 and 12 months was statistically significant compared with baseline (Table 2). When individual comparisons of mean HPD were made for EMD + BG + GTR and BG + GTR with OFD at 12 months, the difference was found to be significantly greater for both groups. There was a statistically significant difference in mean HPD reduction for EMD + BG + GTR when compared with the BG + GTR (Table 3). At 12 months, complete closure of furcation defects was achieved at three sites using EMD + BG + GTR compared with zero using BG + GTR and OFD. The improvement in horizontal classification from

Table 2 Comparison between OFD and test groups at 6- and 12-month follow-ups (mean ± SD)

	PPD (mm)			V-RAL (mm)		
	EMD + BG + GTR	BG + GTR	OFD	EMD + BG + GTR	BG + GTR	OFD
Baseline	3.28 ± 0.76	3.14 ± 0.53	3.02 ± 0.73	11.04 ± 1.57	10.91 ± 0.96	11.61 ± 1.11
6 months	1.86 ± 1.00	2.68 ± 0.66	2.92 ± 0.42	9.36 ± 1.57	10.30 ± 1.14	11.30 ± 1.19
Difference	1.42 ± 1.09*	0.46 ± 0.60*	0.10 ± 0.67	1.68 ± 1.04*	0.61 ± 0.50*	0.31 ± 0.15
12 months	1.54 ± 0.73	2.33 ± 0.81	2.56 ± 0.44	8.92 ± 1.47	10.06 ± 1.23	11.27 ± 1.57
Difference	1.74 ± 1.00*	0.80 ± 0.72*	0.46 ± 0.52*	2.12 ± 1.07*	0.85 ± 0.31*	0.34 ± 0.74

SD = standard deviation; PPD = vertical probing pocket depth; V-RAL = vertical relative attachment level; RGML = relative gingival margin level; HPD = horizontal probing depth; EMD = enamel matrix protein derivative; BG = bone graft; GTR = guided tissue regeneration; OFD = open flap debridement.
*Indicates values that are statistically significant ($P < .05$.).

Table 3 Comparison of results at 12 months (mean ± SD)

Parameters	OFD	BG + GTR (*P*)	EMD + BG + GTR (*P*)	Difference between test groups	*P*
PPD reduction (mm)	0.46 ± 0.52	0.81 ± 0.72 (.025*)	1.74 ± 1.00 (.000*)	0.83 ± 0.29	.011*
CAL gain (mm)	0.34 ± 0.74	0.85 ± 0.31 (.373)	2.12 ± 1.07 (.001*)	1.27 ± 0.35	.002*
GR (mm)	0.12 ± 0.90	0.04 ± 0.49 (.085)	0.37 ± 0.64 (.550)	0.22 ± 0.14	.153
HPD (mm)	0.50 ± 0.70	1.50 ± 0.52 (.002*)	2.10 ± 0.99 (.001*)	0.60 ± 0.35	.109

SD = standard deviation; OFD = open flap debridement; BG = bone graft; GTR = guided tissue regeneration; EMD = enamel matrix protein derivative; PPD = vertical probing pocket depth; CAL = clinical attachment level; GR = gingival recession; HPD = horizontal probing depth.
*Statistically significant ($P < .05$.).

Class II to Class I was observed at seven sites utilizing EMD + BG + GTR, eight utilizing BG + GTR, and two utilizing OFD. However, two sites receiving BG + GTR treatment and eight sites receiving OFD treatment remained unchanged.

Discussion

In the present study, all three groups showed statistically significant PPD reduction 12 months postsurgery. When comparison was made between the three groups, EMD + BG + GTR showed a significantly greater PPD reduction than BG + GTR and OFD. At present, there are no data available on the effects of EMD in combination with GTR membrane and BG for the treatment of Class II furcation defects. The mean PPD reduction observed is comparable with the findings reported in previous studies using EMD alone or in combination with either BG or barrier membrane.[2,19–22] Aimetti et al[21] reported a mean PPD reduction of 1.67 mm at 24 months postsurgery using a combination of EMD with autologous BG for the treatment of Class II furcation defects. Hoffmann et al[20] compared the effectiveness of EMD with bioresorbable membrane in the treatment of Class II furcation defects and reported a greater mean PPD reduction at sites treated with EMD. Casarin et al[22] evaluated the clinical response of EMD for the treatment of Class II furcation defects and reported a mean PPD reduction of 1.71 mm 6 months postsurgery.

RGML (mm)			HPD (mm)		
EMD + BG + GTR	BG + GTR	OFD	EMD + BG + GTR	BG + GTR	OFD
7.75 ± 1.01	7.77 ± 1.07	8.59 ± 0.92	3.30 ± 0.40	3.50 ± 0.70	4.50 ± 1.71
7.50 ± 1.04	7.62 ± 0.96	8.38 ± 1.12	1.60 ± 1.07	2.50 ± 0.70	4.20 ± 1.54
0.25 ± 0.41	0.15 ± 0.68	0.21 ± 0.77	1.70 ± 1.15*	1.00 ± 0.70	0.31 ± 0.48
7.38 ± 1.25	7.73 ± 0.79	8.71 ± 1.30	1.20 ± 0.91	2.00 ± 0.66	4.00 ± 1.24
0.37 ± 0.64	1.04 ± 0.49	0.12 ± 0.90	2.10 ± 0.91*	1.50 ± 0.52*	0.50 ± 0.70

The primary parameter for validation of clinical regeneration after therapy is gain in clinical attachment level (CAL).[23,24] In the present study, EMD + BG + GTR showed a statistically significant CAL gain of 2.12 ± 1.07 mm at 12 months compared to the BG + GTR and OFD. Observations made with regard to CAL gain for EMD + BG + GTR are comparable with results reported in previous studies. Meyle et al[25] evaluated the efficacy of EMD with bioresorbable membrane in the treatment of Class II furcation defects and reported a mean CAL gain of 3.1 mm 14 months postsurgery. Aimetti et al[21] evaluated the effect of EMD with autologous BG for the treatment of Class II furcation defects and reported a mean attachment gain of 2.23 mm at 24 months.

In the present study, significant reductions in mean HPD were observed for EMD + BG + GTR (2.10 mm) as well as BG + GTR (1.5 mm). When comparison was made between these two groups, a significantly greater HPD reduction was observed for EMD + BG + GTR (0.60 mm). Recently, Casarin et al[22] reported reduction of mean horizontal CAL of 1.36 mm at 6 months by using EMD alone for the treatment of Class II furcation defects. The observed significant gains in both horizontal and vertical CAL in the present study, as well as other studies in which EMD was used in combination with BG or GTR, favor the possibility of periodontal regeneration in furcation defects. The advantages of BG and barrier membrane in combination with EMD could be explained by the fact that it might have provided space for regenerating cells and support and protection of the wound at the furcation site during healing.

The main clinical endpoint of any given therapy to treat furcation lesions is the full closure of the furcation, or, if this aim cannot be attained, the conversion from a deep to a shallow lesion.[9] In the present study, the number of Class II furcation defects that closed or converted to Class I were higher for EMD + BG + GTR. Complete furcation closure was observed in 30% (three) and partial closure (Class I) of Class II furcation defects was observed in 70% of cases (seven), while none of the defects remained as Class II in EMD + BG + GTR sites. For BG + GTR sites, partial closure of the furcation was observed in 80% of defects (eight), while 20% of defects (two) remained unchanged. For OFD, partial closure of the furcation was observed in 20% of defects (two), while 80% (eight) remained unchanged. Jepsen et al[2] reported complete furcation closure in 8 of 45 in a group treated by EMD with barrier membrane and 3 of 45 defects in a group treated by barrier membrane alone. Casarin et al[22] evaluated the effectiveness of EMD in the treatment of Class II furcation defects and demonstrated conversion of 67% into Class I, with complete closure in two defects. A major limitation of the present study was that the design of the study did not follow the CONSORT guidelines for clinical trials.

Conclusion

From analysis of the results and within the limitations of the present study, it can be concluded that EMD + BG + GTR and BG + GTR resulted in a statistically significant improvement in terms of V-RAL gain, PPD reduction, and reduction of HPD, and that EMD + BG + GTR resulted in a statistically significant reduction of PPD, V-RAL gain, and a nonsignificantly greater reduction of HPD when compared with BG + GTR.

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