ISSN: 2581-5989
PubMed - National Library of Medicine - ID: 101738774

International Journal of Dental Science and Innovative Research (IJDSIR)
IJDSIR : Dental Publication Service
Available Online at: www.ijdsir.com
Volume – 4, Issue – 5, October - 2021, Page No. : 27 - 38

Clinical and Radiographic Changes in Endo-Periodontal Lesions Managed By Regenerative Periodontal Therapy: An Interdisciplinary 5-Year Retrospective Study

[1]Dr. Anubha Srivastav, MDS, Assistant Professor, Department of Conservative Dentistry and Endodontics, Maharana Pratap Dental College, Kanpur, U.P. India.

[2]Dr. Divya Chowdhary, MDS, Assistant Professor, Department of Conservative Dentistry and Endodontics, Career Post Graduate Institute of Dental Sciences and Hospital, Lucknow , India.

[3]Dr. Amrita Tandon, MDS, Assistant Professor, Department of Pedodontics and Preventive Dentistry, Dental College Azamgarh, U.P. India.

[4]Dr. Rajneesh Maheshwari, MDS, Associate Professor, Department of Periodontics and Oral Implantology, ITS-CDSR, ITS-CDSR, Ghaziabad, U.P. India.

[5]Dr. Mamta Singh, MDS, Assistant Professor, Department of Periodontics and Oral Implantology ITS-CDSR, Ghaziabad-201206, U.P. India.

[6]Dr. Manisha Mallik, MDS, Assistant Professor, Department of Periodontics and Oral Implantology, Buddha Institute of Dental Sciences & Hospital BIDSH, Bihar. India.

Corresponding Author: Dr. Mamta Singh, MDS, Assistant Professor, Department of Periodontics and Oral Implantology ITS-CDSR, Ghaziabad- 201206, U.P. India.

Citation of this Article: Dr. Anubha Srivastav, Dr. Divya Chowdhary, Dr. Amrita Tandon, Dr. Rajneesh Maheshwari, Dr. Mamta Singh, Dr. Manisha Mallik,“Clinical and Radiographic Changes in Endo-Periodontal Lesions Managed By Regenerative Periodontal Therapy: An Interdisciplinary 5-Year Retrospective Study”, IJDSIR- October - 2021, Vol. – 4, Issue - 5, P. No. 27 – 38.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Aim: The goal of this study was to assess clinical and radiographic changes as well as the survival rate in endo-periodontal lesions treated with deproteinized bovine bone mineral (DBBM) with 10% collagen or DBBM with a collagen membrane.

Methodology: This study comprised 52 instances (41 patients) that had been followed for at least 5 years. Periodontal regeneration operations using DBBM with 10% collagen alone or DBBM with a collagen membrane were conducted after scaling and root planing with or without endodontic therapy, resulting in the DBBM + 10% collagen and DBBM + collagen membrane groups, respectively.

The plaque index, bleeding on probing, probing pocket depth, gingival recession, relative clinical attachment level, mobility, and radiographic bone gains were all measured before and after periodontal surgical treatments.

Results: Improvements in clinical indices and radiographic bone growth were reported in both treatment groups at the 12-month follow-up after regeneration operations. The probing pocket depth was reduced more in the DBBM + 10% collagen group (4.521.06 mm) than in the DBBM + collagen membrane group (4.040.82 mm). However, no significant differences existed between the two groups. Furthermore, the radiographic bone growth in the DBBM + 10% collagen group (5.151.54) was equivalent to the DBBM + collagen membrane group (5.351.84). After periodontal regeneration operations, the teeth with endo-periodontal lesions had a 5-year survival rate of 92.31 percent.

Conclusions: The clinical attachment level and radiographic bone level in endo-periodontal lesions were improved by regeneration operations utilizing DBBM with 10% collagen alone, according to this study. Repeated dental hygiene instruction combined with tight supportive periodontal therapy can help to maintain the outcomes of regenerative operations in endo-periodontal diseases.

Keywords: Guided tissue regeneration; Oral hygiene; Periapical periodontitis; Periodontitis; Regenerative endodontics

Introduction

Clinicians have difficulties in accurately diagnosing and treating endo-periodontal lesions. A abnormal connection between the endodontic and periodontal tissues of a single tooth is classified as an endo-periodontal lesion. Bacteria are the primary cause of endodontic and periodontal issues [1-3]. Bacteria and their by-products can be detected in two different types of linkages between pulp and periodontal tissues [2]. The apical foramen, lateral canal, auxiliary foramina, and dentinal tubules are examples of anatomic linkages [2,4]. Root canal or pulp chamber perforation, as well as vertical root fracture or cracking, are the sources of non-physiologic connections [5].

Endo-periodontal lesions, in particular, are characterized by an open wound that necessitates periodontal regeneration therapies. Periapical surgery was found to have a success rate of 27–37 percent in patients with entire apico-marginal buccal bone loss [6,7]. According to Kim et al. [8], the success rate of apico-marginal defects after periapical surgery with a periodontal regeneration treatment was around 73.7 percent after a 5-year follow-up, whereas lesions of purely endodontic origin had a 95.2 percent success rate.

When compared to access flaps, periodontal regenerative procedures using a variety of bone grafts and/or substitutes, root surface demineralization, guided tissue regeneration (GTR), growth and differentiation factors, enamel matrix proteins, or a combination of these have been shown to result in significant probing pocket depth reduction, clinical attachment gain, and hard tissue fill. Deproteinized bovine bone mineral (DBBM) with 10% collagen has been established in several histologic investigations to cause periodontal regeneration [12-14].

The quantity of new bone production was not substantially different between bone grafts without a membrane and those with a membrane, according to Brkovic et al. [16]. In contrast, Lee et al. [17] found that using DBBM and a collagen membrane together resulted in greater new bone production than using DBBM alone. Membrane usage has a number of disadvantages, including a higher risk of infection, gingival recession, and the requirement for a second surgical treatment to remove the non-resorbable membrane [18,19]. In a limited interdental gap or thin biotype, bone grafting paired with a barrier membrane may produce gingival recession, which exposes the membrane and inhibits wound healing.

Materials And Methods

Study population: Ethical approval was taken from Institutional review Board and informed written consent was taken. Patients visiting the Department of Periodontology in collaboration with Department of Conservative Dentistry and Endodontics in a dental college in Uttar Pradesh, India. 20014 to 2019 who met the inclusion criteria were screened for enrollment in this study.

We included adult patients

1) who had received no active maintenance periodontal therapy during the preceding 3 months;
2) one or more periodontal sites with a probing depth ≥5 mm;
3) radiographic evidence of bone loss from marginal bone to root apex;
4) a wide, deep periodontal pocket in 1 tooth surface (grade 2) or deep periodontal pockets in more than 1 tooth surface (grade 3) (for periodontitis patients) [5];
5) at least 2 mm of keratinized tissue; and
6) been complying with a maintenance program.

We excluded patients with diabetes,

1. who were smokers,
2. who had regularly used non-steroidal anti-inflammatory drugs,
3. who had used antibiotics within the previous 3 months,
4. who required antibiotic prophylaxis for therapy,
5. and/or who were pregnant.
6. We also excluded patients who had teeth with horizontal or vertical fractures and iatrogenic root perforation.

Finally, 41 patients with a total of 52 diseased sites requiring periodontal regenerative procedures were included.

Clinical measurements

Plaque index (PI), bleeding on probing (BOP), probing pocket depth (PPD), gingival recession (GR), relative clinical attachment level (RAL), and tooth mobility were all measured at baseline (before periodontal surgery) and 12 months after the surgical treatment. The PPD was calculated as the distance in millimeters from the free gingival border to the base of the likely pocket at six sites per tooth (mesiobuccal, mid-buccal, distobuccal, mesiolingual, mid-lingual, and distolingual) (PCP-UNC 15; Hu-Friedy Mfg. Co., Chicago, IL, USA).

In addition, the PPD measurement for the deepest location (PPDD) was recorded, as well as the associated RAL (RALD). Silness and Löe [21] laid forth a set of criteria for recording the PI. Within 30 seconds after probing the aforementioned 6 locations for the specified research teeth, BOP was judged to be present or missing (+/). Following that, the percent ratio of BOP+ sites to the total of 6 sites was computed. The Periotest value (PTV) was calculated using Periotest Classic to determine the amount of tooth mobility (Medizintechnik Gulden e. K., Modautal, Germany).

Treatment protocol

An overview of the study design is presented as following:

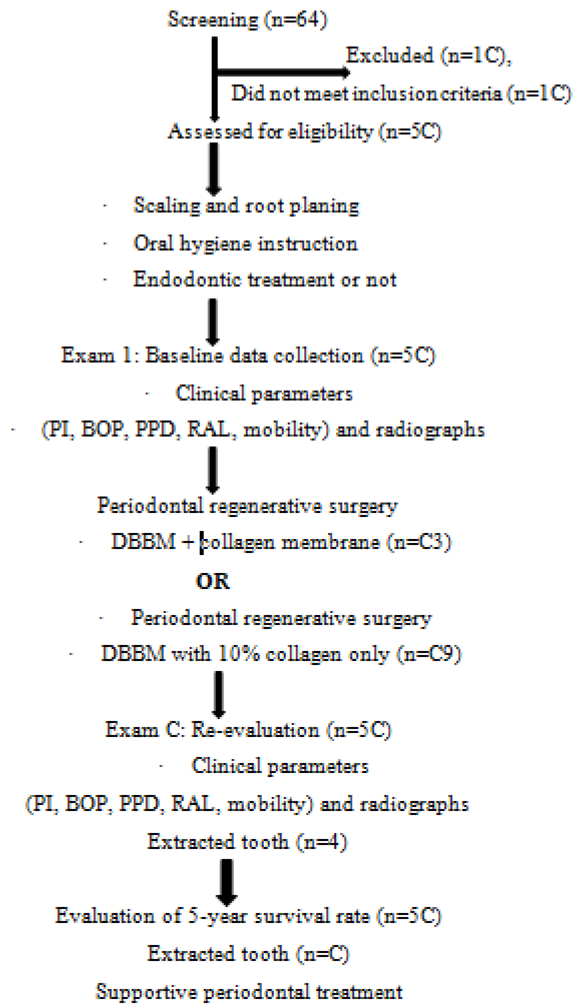

Fig. 1: Flow chart of the participants in this study.

PI: plaque index, BOP: bleeding on probing, PPD: probing pocket depth, RAL: relative clinical attachment level, DBBM: deproteinized bovine bone mineral.

Oral hygiene training was given after scaling and root planing (SRP). The condition of the pulp as well as the quality of the coronal repair were checked. An electric pulp tester (Gentle PulseTM Analog Pulp Vitality Tester, Parkell, Inc., Edgewood, NY, USA) was used to examine the vitality of the affected teeth, and root canal treatment was conducted if the vitality test was negative. The root canals were cleaned and shaped with nickel-titanium rotary devices, and 5.25 percent sodium hypochlorite was used to irrigate them. Gutta-percha and AH Plus sealant were used to close the root canals (Dentsply Maillefer, Tulsa, OK, USA).

Then, using composite resin and stainless steel wire, teeth with mobility higher than degree 1 (PTV 10) were splinted to neighboring teeth.

During the surgical and maintenance phases, splinting was employed to stabilize movable teeth. Three months following root canal therapy, one periodontist (M.S.) conducted periodontal regeneration surgery. Flaps were mirrored with a modified or simpler papilla preservation method based on the diameter of the interdental gap after local anesthesia [22,23]. Then, using composite resin and stainless steel wire, teeth with mobility higher than degree 1 (PTV 10) were splinted to neighboring teeth.

During the surgical and maintenance phases, splinting was employed to stabilize movable teeth. Three months following root canal therapy, one periodontist (M.S.) conducted periodontal regeneration surgery. Flaps were mirrored with a modified or simpler papilla preservation method based on the diameter of the interdental gap after local anesthesia [22,23]. Ultrasonic and hand devices were used to accomplish meticulous degranulation and debridement.

The flaps were repositioned and sutured with 5-0 Nylon (Prolene®, Ethicon Inc., Skillman, NJ, USA) utilizing interrupted suture and horizontal mattress suture procedures. Periodontal surgical techniques were followed by general postoperative guidelines. For 7 days, patients were given oral analgesics (600 mg ibuprofen every 8 hours as needed) and antibiotics (375 mg amoxicillin/clavulanic acid 3 times daily), as well as instructions to rinse with 0.12 percent chlorhexidine gluconate 4 times daily for 3 weeks. Sutures were removed two weeks following surgery.

SPT of the treated teeth was conducted every three months for two years, then every three to six months after that to check clinical and radiographic evidence of healing. Patients were given specific oral hygiene instructions to eliminate supragingival plaque during the maintenance session. Measurements taken by radiography At baseline (before periodontal surgery) and 12 months following the surgical treatment, a digital radiography equipment (CS9300 Select, Carestream Dental LLC., Atlanta, GA, USA) was utilized to capture radiographic images (panoramic and periapical radiographs) of each site.

If there were restorations, the apical border of the restoration was employed as a permanent reference point instead of the CEJ [25]. The BD was defined as the highest apical extension of intrabony damage with normal width periodontal ligament gap. The distance between the CEJ and the BD (CEJ-BD) was measured to determine the degree of radiographic bone gain. By subtracting the baseline value from the 12-month follow-up radiograph, radiographic bone gain was estimated.

As the baseline and 12-month follow-up radiographs were not identical, the vertical distortion between baseline and the 12-month radiographs was estimated as previously described [25,26], by measuring an anatomically non-variable distance such as the root length (distance from the CEJ to the root apex [RA]; CEJ-RA) on both imported images, and a correction factor was calculated as follows: CEJ − RA(baseline) CEJ − RA(12 month radiograph) = Correction factor

The radiographic bone gain at 12 months of follow-up was calculated after applying the correction factor as follows: Radiographic bone gain = [CEJ-BD(baseline)]−[CEJ-BD(12 months)×correction factor]

A single examiner was blinded to the operation and completed all radiographic measures [17]. After a minimum of two weeks, the measurements were redone. Bland-Altman plots and intraclass correlation coefficients were used to assess the repeatability of the two measurements. Additionally, at baseline and 12 months following the surgical treatment, cone-beam computed tomography (CBCT) of the teeth with substantial bone deficiencies was conducted.

Statistical analysis

The data was tested for normality using the Kolmogorov-Smirnov and Shapiro-Wilk tests, and the results showed that the data did not have a normal distribution. All clinical indicators and radiographic bone growth were compared using the Wilcoxon signed rank test between baseline and 12 months after surgery. The Mann-Whitney U test was used to compare changes in clinical indices (PI, BOP, PPD, PPDD, GR, RAL, RALD, and mobility) and radiographic bone growth according to treatment mode. Spearman correlation coefficients were used to analyze the relationship between radiographic bone growth and the kind of bone defect.

Results

At the baseline and 12-month follow-up, a total of 52 cases (41 patients) were assessed. The average duration of follow-up was 70.0817.21 months (range: 59–122 months). The demographic data of the patients is shown in Table 1: At 5 years after periodontal regeneration operations, the survival percentage of teeth with endoperiodontal lesions was 92.31 percent.

Variables	No.
Sex	
Male	20
Female	32

Sites		
Mx. anterior area	4	
Mx. premolar area	4	
Mx. posterior area	24	
Mn. anterior area	5	
Mn. premolar area	3	
Mn. posterior area	12	
Defect type		
1-wall	34	
2-wall	18	
3-wall	0	
Endodontic treatment		
Yes	45	
No	7	
Guided tissue regeneration		
Yes	23	
No	29	
New prosthesis		
Yes	40	
No	12	
Survived teeth	46	
Extracted teeth	6	
Due to fracture	3	
Due to improper oral hygiene	1	
Due to endodontic failure	1	
Due to strategic reasons	1	
Follow-up period (mean ± SD, mon)	70.08 ±	17.21
Survival period (mean ± SD, mon)	66.77 ±	19.12

Table 1 shows the demographic information of the patients.

The clinical parameters obtained at baseline and the 12-month follow-up are presented in Table 2.

Variables	Baseline	12-month follow-up	Difference	P value
PI	1.06±0.29	0.74±0.22	0.32±0.27	<0.001
BOP (%)	48.08±9.71	13.78±6.37	34.29±10.13	<0.001
PPD (mm)	5.14±0.83	2.96±0.31	2.19±0.71	<0.001

PPDD (mm)	7.59±0.89	3.35±0.48	4.31±0.98	<0.001
GR (mm)	1.43±0.58	2.20±0.77	0.77±0.34	<0.001
RAL (mm)	6.58±0.99	5.16±0.77	1.42±0.76	<0.001
RALD (mm)	9.03±1.01	5.49±1.05	3.54±1.03	<0.001
Mobility (PTV)	26.42±2.28	10.27±2.04	16.15±2.46	<0.001
CEJ-BD (mm)	9.82±1.44	4.58±1.06	5.24±1.67	<0.001

Table 2: Comparison of clinical parameters and radiographic bone gain between baseline and the 12-month follow-up

From baseline to the 12-month follow-up, PI, BOP, and mobility considerably decreased (P0.001), but GR significantly increased (P0.001). By 12 months following the periodontal regeneration treatment, PPD and RAL had greatly improved. For the radiographic assessment, the correction factor was 1.000.02. The radiography measures' Bland-Altman graphs revealed high agreement. The baseline and 12-month follow-up intraclass correlation coefficients for radiographic measures were 0.927 and 0.982, respectively. Table 3 shows the changes in clinical parameters and radiographic bone gain as a function of treatment mode.

Variables	No.	ΔPPD	ΔPPDD	ΔRAL	ΔRALD	ΔMobility	ΔCEJ-BD
Membrane							
Yes	23	2.12±0.75	4.04±0.82	1.41±0.84	3.33±0.89	16.48±2.86	5.35±1.84
No	29	2.24±0.69	4.52±1.06	1.43±0.70	3.71±0.12	15.89±2.11	5.15±1.54
P value		0.607	0.071	0.264	0.36	0.232	0.416
Endodontic treatment							
Yes	45	2.19±0.72	4.44±0.97	1.43±0.79	3.68±1.02	16.36±2.27	5.30±1.73
No	7	2.17±0.68	3.43±0.53	1.38±0.56	2.64±0.56	14.86±3.39	4.83±1.19
P value		0.958	0.009[a)]	0.916	0.007[a)]	0.356	0.581
New prosthesis							
Yes	40	2.30±0.72	4.38±1.01	1.58±0.76	3.65±1.07	16.28±2.31	5.48±1.72
No	12	1.82±0.56	4.08±0.90	0.90±0.51	3.17±0.83	15.75±2.99	4.45±1.25
P value		0.046[b)]	0.339	0.005[a)]	0.14	0.361	0.043[b)]
Total	52	2.19±0.71	4.31±0.98	1.42±0.76	3.54±1.03	1.94±0.46	5.24±1.67

Table 3: Comparison of clinical parameters and radiographic bone gain according to treatment modality.

At 12 months following periodontal regeneration operations, PPDD decrease was larger in the bone-grafted teeth without membranes (4.521.06 mm) than in the bone-grafted teeth with membranes (4.040.82 mm) among the treatment-related factors. The bone-grafted teeth with membranes and the bone-grafted teeth without membranes, on the other hand, showed no significant difference. Furthermore, the change in CEJ-BD between the bone-grafted teeth with membranes (5.351.84 mm) and the bone-grafted teeth without membranes (5.151.54 mm) at the 12-month follow-up was identical. The relationships between clinical indicators were also investigated (Table 4).

PPDD decrease was substantially associated to the change in PI between baseline and 12-month follow-up (Spearman correlation coefficient=0.422, P=0.002). Furthermore, there was a significant association between RALD gain and PI decrease between baseline and 12-month follow-up (Spearman correlation coefficient=0.398, P=0.003). The reduction in CEJ-BD was shown to be substantially linked with the kind of bone defect (Spearman correlation coefficient=0.334, P=0.016).

Discussion

In the current investigation, periodontal regeneration therapy with DBBM containing 10% collagen but not a collagen membrane resulted in increased clinical attachment level and radiographic bone growth in endo-periodontal lesions. All clinical indicators were greatly improved in this trial, including PPDD, RALD, mobility, BOP, and CEJ-BD. The goals of periodontal regeneration therapies are to improve the periodontal attachment and bone volume of a severely deteriorated tooth, reduce PPD, and reduce GR [10].

Since the early 1970s, bone grafts and/or replacements, root surface demineralization, GTR, growth and differentiation factors, enamel matrix proteins, and various combinations thereof have been employed to achieve predictable periodontal regeneration [11]. In this investigation, we employed either DBBM without a collagen membrane or DBBM with a collagen membrane. With a modified papilla preservation flap, we inserted a collagen membrane when the interdental gap width was >2 mm.

After employing DBBM with or without collagen membranes, the breadth of the interdental gap was new cementum next to the graft. In addition, another study found that using DBBM with 10% collagen resulted in histologic indications of regeneration [12]. The researchers demonstrated the efficiency of DBBM for periodontal regeneration when combined with either 10% collagen or a collagen membrane. Hartman et al. [14] found that using DBBM with a collagen membrane did not improve periodontal regeneration. Similarly, no statistically significant changes in clinical attachment level or radiographic bone growth were found between the groups with and without membranes in the current investigation.

In a recent comprehensive study, it was discovered that in situations of nonguided tissue regeneration, a lengthy junctional epithelium was not always generated [11]. The absence of epithelial downgrowth may not be the most important factor in new connective tissue attachment (e.g., the GTR principle). This finding shows that wound stability and space are critical for the periodontium's natural healing capability to be realized.

In endo-periodontal lesions, this study found a tooth survival rate of 92.31 percent at 5 years after a periodontal regeneration surgery. This finding is consistent with a previous comprehensive study that found a survival rate of 72.1 percent to 100 percent for teeth with endo-periodontal lesions [30]. At the 13-month, 31-month, and 42-month follow-up visits, three of the six failed teeth were taken due to breakage. At a 49-month follow-up appointment, a mandibular second molar with growing apical radiolucency and greater mobility was similarly excised without endodontic treatment.

A maxillary first molar with an endodontic issue was removed, with the source of infection being a fourth canal with inadequate root canal therapy. We believe that a protracted periodontal infection combined with the pulp's defensive mechanism restricted the root canal, resulting in the return of an endo-periodontal lesion 6 years after the periodontal regeneration operation. After 11 years of follow-up, a maxillary central incisor that had shown outstanding radiographic bone healing was excised for strategic reasons.

Surprisingly, following extraction, we found bone adhering to the root. This tooth had ankylosis-like recovery and good bone growth next to DBBM particles. We believe the healing-like ankylosis was caused by vigorous root planing and degranulation of diseased tissue during surgery, or by splinting the treated teeth over the 12-month healing period. Before periodontal regeneration operations, we used resin and stainless-steel wire to splint teeth with mobility greater than degree 1 (PTV10) with neighboring teeth. We re-evaluated the teeth and removed the resin-wire splint during the 12-month follow-up.

Despite the fact that the impact of tooth mobility on regenerative therapy is debatable, some research has indicated that splinting movable teeth prior to a regenerative operation aids wound healing [31-33].

The size and shape of the lesion, the patient's smoking behaviors, and oral hygiene compliance are all factors that impact the outcome of periodontal regeneration treatments [18,19,34]. After the periodontal regeneration treatment, supportive periodontal maintenance care is crucial for the long-term effectiveness of periodontal therapy. Oral hygiene compliance and smoking behaviors are key drivers among patient-related variables [34].

All of the participants in this research did not smoke, had a good compliance with periodontal maintenance regimens, and had no relevant medical history. Bone grafting operations using DBBM were conducted in 1-wall defects, as well as 2- and 3-wall intrabony defects, in this study. The kind of lesion had a substantial impact on radiographic bone gain. Furthermore, an increase in PI was linked to a decrease in PPDD and an increase in RALD. Despite the efficacy of the periodontal regeneration methods, the final outcome of periodontal repair is largely dependent on the patients' dental hygiene and compliance with SPT.

With the higher success rate of implants, periodontists are having a hard time deciding whether to extract severely periodontally affected teeth with endodontic issues. Despite the fact that teeth with a severe intrabony defect have a 96 percent survival probability for up to 15 years [10], survival can be achieved with ongoing oral hygiene education and expert tooth cleaning under a strict recall program. As a result, 12 months following the periodontal regeneration operation, we re-evaluated the teeth to see if they needed a new prosthesis. We also told the patients that oral hygiene compliance is crucial to the longevity of the treated tooth.

Other important elements to consider are patient participation, restorability, and the patient's financial situation, all of which impact treatment options [2]. New prosthesis improved patients' oral hygiene in some circumstances by modulating the embrasure space and the cervical region of teeth, which were previously difficult to clean well. If the treated tooth was splinted with the neighboring tooth, a new prosthesis might increase its stability.

Limitations

There are various limitations to this study. Firstly, retrospective studies are prone to bias. Second, we have to consider cost and patient preferences while evaluating the efficacy of membrane usage, endodontic therapy, and new prosthetic treatment. The research, on the other hand, offered a number of advantages. To begin, just one periodontist conducted all periodontal regenerative therapies (M.S.). Second, we advised patients to brush and floss their teeth properly before and after the periodontal restorative operations. Every visit before and shortly after surgery, as well as during SPT, all patients' oral hygiene condition was assessed using a disclosing solution.

As a result, local and general infection sources might be reduced. Third, following periodontal regeneration operations, 40 teeth were repaired with new prostheses. Fourth, we looked at the survival rate and causes for failure in teeth with endo-periodontal issues that were substantially damaged. Finally, 11-year histological follow-up outcomes of DBBM with 10% collagen in endo-periodontal lesions were published in this work.

Conclusion

The clinical attachment level and radiographic bone level in endo-periodontal lesions were improved by periodontal regeneration operations utilizing DBBM with 10% collagen alone, according to this study. In situations with apical involvement, we believe that endodontic therapy prior to the ultimate periodontal regeneration operation promotes periodontal recovery. Repeated oral hygiene instruction within a stringent SPT program is critical for optimal maintenance of the effects of periodontal regeneration operations in endo-periodontal diseases.

References

1. Löe H, Theilade E, Jensen SB. Experimental gingivitis in man. J Periodontol 1965;36:177-87.
2. Zehnder M, Gold SI, Hasselgren G. Pathologic interactions in pulpal and periodontal tissues. J Clin Periodontol 2002;29:663-71.
3. Fabricius L, Dahlén G, Sundqvist G, Happonen RP, Möller AJ. Influence of residual bacteria on periapical tissue healing after chemomechanical treatment and root filling of experimentally infected monkey teeth. Eur J Oral Sci 2006;114:278-85.
4. Simon JH, Glick DH, Frank AL. The relationship of endodontic-periodontic lesions. J Periodontol 1972;43:202-8.
5. Herrera D, Retamal-Valdes B, Alonso B, Feres M. Acute periodontal lesions (periodontal abscesses and necrotizing periodontal diseases) and endo-periodontal lesions. J Periodontol 2018;89 Suppl 1:S85-102.
6. Hirsch JM, Ahlström U, Henrikson PA, Heyden G, Peterson LE. Periapical surgery. Int J Oral Surg 1979;8:173-85.
7. Skoglund A, Persson G. A follow-up study of apicoectomized teeth with total loss of the buccal bone plate. Oral Surg Oral Med Oral Pathol 1985;59:78-81.
8. Kim E, Song JS, Jung IY, Lee SJ, Kim S. Prospective clinical study evaluating endodontic microsurgery outcomes for cases with lesions of endodontic origin compared with cases with lesions of combined periodontal-endodontic origin. J Endod 2008;34:546-51.
9. Kao RT, Nares S, Reynolds MA. Periodontal regeneration-intrabony defects: a systematic review from the AAP Regeneration Workshop. J Periodontol 2015;86 Suppl:S77-104.
10. Cortellini P, Tonetti MS. Clinical concepts for regenerative therapy in intrabony defects. Periodontol 2000 2015;68:282-307.
11. Sculean A, Nikolidakis D, Nikou G, Ivanovic A, Chapple IL, Stavropoulos A. Biomaterials for promoting periodontal regeneration in human intrabony defects: a systematic review. Periodontol 2000 2015;68:182-216.
12. Nevins ML, Camelo M, Lynch SE, Schenk RK, Nevins M. Evaluation of periodontal regeneration following grafting intrabony defects with bio-oss collagen: a human histologic report. Int J Periodontics Restorative Dent 2003;23:9-17.
13. Sculean A, Stavropoulos A, Windisch P, Keglevich T, Karring T, Gera I. Healing of human intrabony defects following regenerative periodontal therapy with a

bovine-derived xenograft and guided tissue regeneration. Clin Oral Investig 2004;8:70-4.
14. Hartman GA, Arnold RM, Mills MP, Cochran DL, Mellonig JT. Clinical and histologic evaluation of anorganic bovine bone collagen with or without a collagen barrier. Int J Periodontics Restorative Dent 2004;24:127-35.
15. Guillemin MR, Mellonig JT, Brunsvold MA. Healing in periodontal defects treated by decalcified freeze-dried bone allografts in combination with ePTFE membranes (I). Clinical and scanning electron microscope analysis. J Clin Periodontol 1993;20:528-36.
16. Brkovic BM, Prasad HS, Rohrer MD, Konandreas G, Agrogiannis G, Antunovic D, et al. Beta-tricalcium phosphate/type I collagen cones with or without a barrier membrane in human extraction socket healing: clinical, histologic, histomorphometric, and immunohistochemical evaluation. Clin Oral Investig 2012;16:581-90.
17. Lee JS, Jung JS, Im GI, Kim BS, Cho KS, Kim CS. Ridge regeneration of damaged extraction sockets using rhBMP-2: an experimental study in canine. J Clin Periodontol 2015;42:678-87.
18. Becker W, Becker BE. Clinical applications of guided tissue regeneration: surgical considerations. Periodontol 2000 1993;1:46-53.
19. Villar CC, Cochran DL. Regeneration of periodontal tissues: guided tissue regeneration. Dent Clin North Am 2010;54:73-92.
20. Anderegg CR, Metzler DG, Nicoll BK. Gingiva thickness in guided tissue regeneration and associated recession at facial furcation defects. J Periodontol 1995;66:397-402.
21. Silness J, Löe H. Periodontal disease in pregnancy. II. Correlation between oral hygiene and periodontal condition. Acta Odontol Scand 1964;22:121-35.
22. Cortellini P, Prato GP, Tonetti MS. The modified papilla preservation technique. A new surgical approach for interproximal regenerative procedures. J Periodontol 1995;66:261-6.
23. Cortellini P, Prato GP, Tonetti MS. The simplified papilla preservation flap. A novel surgical approach for the management of soft tissues in regenerative procedures. Int J Periodontics Restorative Dent 1999;19:589-99.
24. Björn H, Halling A, Thyberg H. Radiographic assessment of marginal bone loss. Odontol Revy 1969;20:165-79.
25. Liñares A, Cortellini P, Lang NP, Suvan J, Tonetti MS; European Research Group on Periodontology (ErgoPerio). Guided tissue regeneration/deproteinized bovine bone mineral or papilla preservation flaps alone for treatment of intrabony defects. II: radiographic predictors and outcomes. J Clin Periodontol 2006;33:351-8.
26. Tonetti MS, Pini Prato G, Williams RC, Cortellini P. Periodontal regeneration of human infrabony defects. III. Diagnostic strategies to detect bone gain. J Periodontol 1993;64:269-77.
27. Camelo M, Nevins ML, Schenk RK, Simion M, Rasperini G, Lynch SE, et al. Clinical, radiographic, and histologic evaluation of human periodontal defects treated with Bio-Oss and Bio-Gide. Int J Periodontics Restorative Dent 1998;18:321-31.
28. Paolantonio M, Scarano A, Di Placido G, Tumini V, D'Archivio D, Piattelli A. Periodontal healing in humans using anorganic bovine bone and bovine peritoneum-derived collagen membrane: a clinical and

histologic case report. Int J Periodontics Restorative Dent 2001;21:505-15.

29. Camelo M, Nevins ML, Lynch SE, Schenk RK, Simion M, Nevins M. Periodontal regeneration with an autogenous bone-Bio-Oss composite graft and a Bio-Gide membrane. Int J Periodontics Restorative Dent 2001;21:109-19.
30. Schmidt JC, Walter C, Amato M, Weiger R. Treatment of periodontal-endodontic lesions--a systematic review. J Clin Periodontol 2014;41:779-90.
31. Schulz A, Hilgers RD, Niedermeier W. The effect of splinting of teeth in combination with reconstructive periodontal surgery in humans. Clin Oral Investig 2000;4:98-105. 32.
32. Cortellini P, Stalpers G, Mollo A, Tonetti MS. Periodontal regeneration versus extraction and prosthetic replacement of teeth severely compromised by attachment loss to the apex: 5-year results of an ongoing randomized clinical trial. J Clin Periodontol 2011;38:915-24.
33. Siciliano VI, Andreuccetti G, Siciliano AI, Blasi A, Sculean A, Salvi GE. Clinical outcomes after treatment of non-contained intrabony defects with enamel matrix derivative or guided tissue regeneration: a 12-month randomized controlled clinical trial. J Periodontol 2011;82:62-71.
34. Cortellini P, Paolo G, Prato P, Tonetti MS. Long-term stability of clinical attachment following guided tissue regeneration and conventional therapy. J Clin Periodontol 1996;23:106-11.