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EFFECT OF ENAMEL MATRIX PROTEIN DERIVATIVE (EMD) AS AN ADJUNCT TO XENOGRAFT COMPARED TO XENOGRAFT ALONE IN THE TREATMENT OF INTRABONY DEFECTS IN SUBJECTS WITH CHRONIC PERIODONTITIS: A SYSTEMATIC REVIEW.

Dentistry

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ABSTRACT

Background: Enamel matrix derivative (EMD) has been widely used in periodontal regenerative treatment and the xenograft biomaterials show good biocompatibility and osteoconductivity of demineralized bovine bone matrix. So, to evaluate the improvement in clinical outcomes when Enamel Matrix Protein Derivative is used as an adjunct to Bovine-Derived Xenograft in intrabony defects of chronic periodontitis patients. **Material And Methodology:** In this systematic review, randomized controlled trials in subjects with periodontitis in the age group of 25-70 years were considered. An electronic search was made in PubMed, Google Scholar, and EMBASE databases. Studies concerning the use of a combination of enamel matrix derivative (EMD) and Xenograft compared with xenografts alone in periodontitis treatment were selected. **Result:** 4 studies were included in quantitative analysis after screening by two reviewers. Randomized controlled trials have indicated a significantly higher pocket reduction and clinical attachment level gain after the application of enamel matrix derivative (EMD) and Xenograft compared with xenografts alone. **Conclusion:** The use of enamel matrix derivative (EMD) as an adjunct to Xenograft provides significant results as compared to xenograft alone in intrabony defects of chronic periodontitis patients.

KEYWORDS

Enamel matrix protein derivative (EMD), Xenograft, Intrabony defects, Chronic periodontitis.

INTRODUCTION:

Periodontitis is an infectious disease that is caused by periodontal pathogenic bacteria and is characterized by pocket formation and attachment loss, ultimately affecting tooth survival.[5]

The bone replacement graft provides for regeneration through osteoconductive or osteoinductive processes and growth factors by inductive or cell-stimulating mechanisms.[1] The osteoconductive graft acts as a scaffold to support new tissue growth. The inductive process involves the graft or growth factor stimulating the host tissues to regenerate lost structures.[1]

Enamel matrix protein derivative (EMD), derived from developing porcine teeth consists of 90% amelogenins, with the remaining 10% primarily proline-rich non-amelogenins, tuftelin, tuft protein, serum, ameloblastin, amelin, and salivary proteins[3]. It induces the expression of cementogenesis - and osteogenesis-related genes in the mesenchymal cells, and has been used as an osteo-promotive agent for the regeneration of damaged periodontal support structures for >20 years.[1]

Demineralized porcine bone matrix (DPBM) is one of the most successfully used xenografts in various periodontal and implant surgeries including guided bone regeneration, alveolar ridge preservation, and sinus augmentation, and provides stable and reliable results clinically and radiographically. The good biocompatibility and osteoconductivity of demineralized bovine bone matrix, which is one of the most studied and accepted xenograft biomaterials. It has been widely used to improve the results of regenerative treatment in combination with EMD.

Thus, from both a biological as well as a clinical point of view, it would be pertinent to evaluate the combination of EMD and a bone graft as a treatment of advanced intrabony defects.

Protocol And Registration:

This systematic review is registered on the PROSPERO website: CRD420234929

This systematic review is according to PRISMA guidelines.

Focused Question

What are the clinical benefits of using a combination of enamel matrix derivative (EMD) and Xenograft compared with xenografts alone in subjects with chronic periodontitis with intrabony defects?

Population (P) – Subjects with chronic periodontitis

Intervention (I) – Combination of enamel matrix derivative (EMD) and
Xenograft Comparison (C) – Xenograft alone Outcome (O)- Reduction in probing pocket depth (PPD) and gain in clinical attachment level (CAL)

METHOD:

Inclusion Criteria: -

1. Randomized controlled trials comparing EMD + xenograft with xenograft alone
2. Studies with a mean follow-up period between 6 months and 4 years
3. Defect sites with pocket depth (PD) ≥5 mm & Intrabony defect depth ≥3 mm
4. Studies published in English language only from year January 2002 to May 2022
5. Patients with moderate to severe periodontitis

Exclusion Criteria: -

Review papers, In- vitro studies, animal studies, case reports, commentaries, and interviews.

Information Source:

A literature search was performed in PubMed, PMC, Google scholar, and EBSCO host databases for papers published from 2002 up to September 2022.

Search Strategy:

Papers published in the English language were selected for analysis.

Keywords used for study identification in all databases were "(enamel matrix derivative AND Xenograft) AND intrabony defect" and "(enamel matrix derivative) AND (xenograft) AND periodontal disease AND intrabony defect.

Selection Process:

1. Assessment of titles and abstracts

2. Assessment of full-text

Data Collection Process:
Data extraction sheet was prepared based on variables and the articles were analysed. Using data extraction sheet, the following data were collected: authors, year of publication, country, aim, tissue assessed, type of study, sample size, comparison group & control group, methodology, and conclusion. (Fig.1)

Data Items:
Variables for which data was sought included Periodontal disease, periodontitis, gingivitis, clinical attachment level, and pocket depth.

RESULTS:
Study Selection
A total of 1343 articles were found after electronic search. 1291 articles, which were of other languages and duplicates, were excluded leaving 52 articles. 42 articles were excluded after reviewing the abstracts leaving 10 articles .6 articles were excluded as they did not fulfil the eligibility criteria leaving 4 articles for this systematic review.

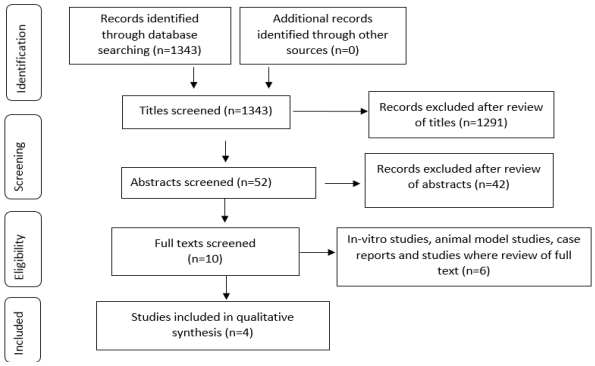


Figure 1- Flow Chart Of Literature Search Results And Study Selection

Study Characteristics
An overview of the included studies for the analysis is presented in Table 1.

Table 1: Studies Included In The Review:

Sr No	Author, Year	Title	Test Group	Control Group	Study Design	Follow Up	Results
1	Sculean.A. et al;2002	Clinical Evaluation of an Enamel Matrix Protein Derivative (Emdogain) Combined with a Bovine-Derived Xenograft (Bio-Oss) for the Treatment of Intrabony Periodontal Defects in Humans	Intrabony defect, were randomly treated with a combination of EMD + BDX	BDX alone	RCT	1 year	Both therapies led to significant improvements of the investigated clinical parameters.
2	Scheyer ET;2002	A clinical comparison of a bovine-derived xenograft used alone and in combination with enamel matrix derivative for the treatment of periodontal osseous defects in humans	Combination of EMD and BDX	BDX alone	RCT	6 months	The particulate anorganic cancellous bovine-derived bone xenograft used alone and in combination with enamel matrix derivative are effective for the treatment of human intrabony periodontal lesions
3	Lee JH, et al;2020	Adjunctive use of enamel matrix derivatives to porcine-derived xenograft for the treatment of one-wall intrabony defects: Two-year longitudinal results of a randomized controlled clinical trial.	DPBM with the adjunctive use of EMD	DPBM only	RCT	2 years	DPBM has been verified for biocompatibility and can be used as a scaffold to enhance the clinical and radiographic outcomes of periodontal regeneration of one-wall intrabony defects. In particular, the adjunctive use of EMD significantly reduced the postoperative discomfort
4	Lee JH.et al;2022	Long term stability of adjunctive use of enamel matrix protein derivative on porcine-derived xenograft for the treatment of one-wall intrabony defects: A 4-year extended follow-up of a randomized controlled trial	DPBM with the adjunctive use of EMD	DPBM only	RCT	4 years	The clinical, radiographic, and patient-reported outcomes were significantly improved when DPBM was used in the regenerative treatment, but no additional benefits were observed with the adjunctive use of EMD

Risk Of Bias In Individual Studies:
This assessment was conducted by using the recommended approach for assessing the risk of bias in studies included in Cochrane Reviews (Higgins 2011)[22] using the tool RevMan 5.0.

We used the two-part tool to address the six specific domains (namely: random sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other bias). Each domain includes one or more specific entries in a Risk of Bias table. Within each entry, the first part of the tool involves describing what was reported to have happened in the study.

The second part of the tool involves assigning a judgment relating to the risk of bias for that entry: either low risk, unclear risk, or high risk.

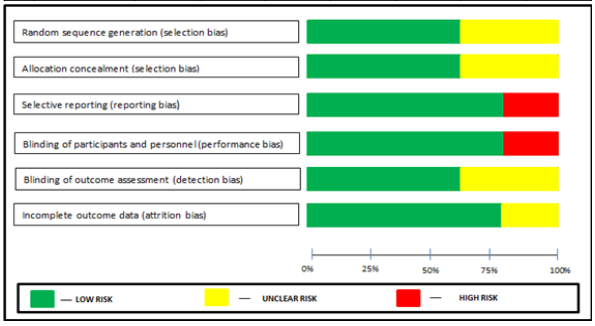
The domains of random sequence generation, allocation concealment, blinding, incomplete outcome data, and selective reporting are addressed in the tool by a single entry for each study. We completed a Risk of bias table for each included study.

The risk of bias of the included studies is presented in Table 2, graph 1, and graph 2.

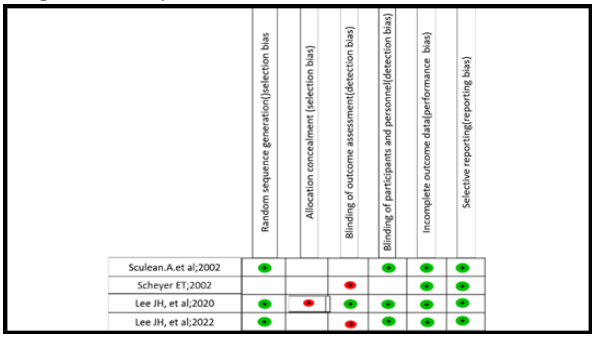
Table 2: Quality Assessment Of The Studies Included By Judging Risk Of Bias And Applicability Using Cochrane Risk Of Bias Tool For Randomized Controlled Trial

Sr no	Author /year	Type of study	Random sequence generation	Allocation concealment	Blinding of participants	Blinding of outcome	Incomplete outcome data	Selective reporting
1.	Anton Sculean, et.al;2002	RCT	Low	Low	Low	Unclear	Unclear	Unclear
2.	Scheyer ET, et.al;2002	RCT	Low	Unclear	Unclear	Unclear	Low	Low

3.	Lee JH, Kim DH, et.al;2020	RCT	Low	Low	Low	Low	Low	Uncle ar
4.	Lee JH, Jeong SN;2022	RCT	Low	Low	Low	Low	Low	Uncle ar



Graph 1: Summary Of Risk Of Bias Assessment Of Selected Studies



Graph 2: Summary Of Risk Of Bias Assessment Of Individual Studies

DISCUSSION:

Periodontitis, an infectious disease characterized by progressive attachment and bone degeneration, may ultimately result in tooth loss if left untreated. Results from a national survey conducted in the United States in 2009 and 2010 demonstrated that over 47% of the adult population aged 30 years and above had periodontitis, distributed as 8.7%, 30.0%, and 8.5% with mild, moderate, and severe periodontitis, respectively. Regenerative periodontal surgery aims to predictably restore the tooth's supporting apparatus (i.e., root cementum, periodontal ligament, and bone) that has been lost following periodontal disease or trauma.[6]

Enamel matrix derivative (EMD) has been widely used in periodontal regenerative treatment, especially for contained intrabony periodontal defects. Among the bone grafting biomaterials that are successfully used as scaffolds with EMD deproteinized bovine bone mineral (DBBM) shows an additional improvement in clinical outcomes when combined with EMD and is considered effective especially in large or non-contained intrabony defects.

In the present review, studies in which xenograft was used along with other agents were excluded.

Matarasso M.et al, 2015 conducted a systematic review on Enamel matrix derivative and bone grafts for periodontal regeneration of intrabony defects. Concluded that the combination of EMD and bone grafts may result in additional clinical improvements in terms of CAL gain and PD reduction compared with those obtained with EMD alone. Lee JH et al (2019) shows that no statistically significant differences regarding any early clinical complication including dehiscence/fenestration, persistent swelling, spontaneous bleeding, and ulceration were observed between the control and test groups. Although these findings confirm the tendency of the adjunctive use of EMD to promote periodontal regeneration and reduce postoperative discomfort, it is difficult to definitively make this conclusion, given the data provided in the study.

Scheyer ET (2002), This study compared enamel matrix derivative (EMD) combined with a particulate anorganic cancellous bovine-derived bone xenograft (BDX) to BDX alone in the treatment of human intrabony defects. The results of this study demonstrate that both treatment modalities provide improvements in hard and soft tissue measurements that are statistically and clinically significant when compared to baseline. Furthermore, statistical analysis of the data revealed no significant differences between the treatment groups. Sculean A et al (2002), The results of this study have demonstrated that treatment of deep intrabony defects with both the combination of EMD + BDX and BDX alone may lead to clinically and statistically significant PPD reduction and CAL gain. No statistically or clinically significant differences in any of the investigated parameters were observed between the two treatments.

Limitations:

There are limited studies which is available. Also, there is a lack of data evaluating the long term follow up of the intervention. There can be selection bias as there is no consideration of multicentred clinical trials.

Implications Of The Results For Practice:

Xenografts can be used along with EMD in the clinical practice for the treatment of patients with moderate to severe periodontitis as they show positive results.

Future Research:

Studies can be carried out with different material combination with xenografts and EMD.

CONCLUSION:

Xenografts are biocompatible and can be used as a scaffold to enhance the clinical and radiological outcomes of periodontal regeneration of one-wall intrabony defects. In particular, the adjunctive use of EMD in combination with DPBM significantly reduced postoperative discomfort when compared with DPBM without EMD. DPBM is biocompatible and can be used as a scaffold to enhance the clinical and radiological outcomes of periodontal regeneration of one-wall intrabony defects, with greater knowledge and understanding of the biological effects that mediators such as EMD can produce, future outcomes in new levels of success and predictability.

Support:

No source of funding.

Conflicts Of Interest:

No conflicts of interest.

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