International Journal of Dental Research and Allied Sciences
2023, Volume 3, Issue 1, Page No: 94-104

Available online at: www.tsdp.net

ISSN: 3062-3502

Review Article

A Systematic Review of Enamel Matrix Derivatives as a Supplement to Alveolar Ridge Preservation

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Received: 07 February 2023; **Revised:** 19 May 2023; **Accepted:** 24 May 2023

ABSTRACT

This systematic review aimed to evaluate existing evidence on the use of enamel matrix derivatives (EMDs) as an adjunctive therapy in alveolar ridge preservation (ARP) following tooth extraction. An extensive search was performed across MEDLINE, the Cochrane Library, PsycINFO, Web of Science, Google Scholar, and Scopus to locate randomized controlled clinical trials (RCTs) relevant to this topic. The main outcomes assessed included histomorphometric and radiographic parameters, while secondary outcomes involved implant placement feasibility and patient-centered factors such as postoperative discomfort. From 436 studies published between 2011 and 2022, only five met the inclusion criteria, encompassing a total of 146 patients. Owing to considerable variability across studies, a meta-analysis was not feasible. Qualitative assessment revealed slight improvements, including a higher proportion of new bone formation and reduced postoperative discomfort following extraction. Although EMDs have demonstrated regenerative benefits in other dental applications, their adjunctive use in ARP warrants further exploration. Additional well-designed randomized clinical trials are essential to clarify their precise efficacy and clinical relevance.

Keywords: Dental implant, Enamel matrix derivatives, Alveolar ridge preservation, Tooth extraction, Bone regeneration

How to Cite This Article: Seo yeon P, Ji min C, Soo bin J. A Systematic Review of Enamel Matrix Derivatives as a Supplement to Alveolar Ridge Preservation. Int J Dent Res Allied Sci. 2023;3(1):94-104. https://doi.org/10.51847/5iNDxybWev

Introduction

In most clinical situations, the decision to extract a tooth is closely linked to planning for its replacement. This process involves considering multiple factors, including the available treatment options, their respective benefits and limitations, and the preferences of both the clinician and the patient [1]. Among the available restorative methods, dental implant therapy is widely regarded as an effective solution for replacing missing teeth, restoring both function and esthetics [2]. Successful outcomes with this treatment require a thorough understanding of the biological processes underlying post-extraction tissue remodeling, implant osseointegration, and the application of tissue engineering techniques to ensure long-term stability [3, 4].

Because the alveolar bone proper and periodontal ligament depend on the presence of a tooth, their loss following extraction leads to substantial bone resorption due to natural remodeling and the absence of functional stimulation [5]. This bone reduction, particularly in the anterior region, may complicate implant placement by necessitating bone augmentation, limiting prosthetically guided implant positioning, and compromising esthetic outcomes, while also contributing to other clinical and patient-related challenges [6, 7]. A systematic review that included 20 studies estimated the average dimensional changes in the alveolar ridge following unassisted socket healing [8]. The analysis found that, in molar sites, mean horizontal reduction was 3.61 mm (95% CI: 3.24–3.98), vertical mid-facial reduction was 1.46 mm (95% CI: 0.73–2.20), and mid-lingual reduction was

1.20 mm (95% CI: 0.56–1.83). In non-molar regions, mean reductions were 2.54 mm (95% CI: 1.97–3.11), 1.65 mm (95% CI: 0.42–2.88), and 0.87 mm (95% CI: 0.36–1.38), respectively [8].

Alveolar ridge preservation (ARP) has been developed as a preventive strategy to mitigate post-extraction bone resorption and preserve esthetics [9]. Numerous grafting materials have been proposed for ARP, including autologous bone, allografts, xenografts, alloplasts, and biologic agents. Despite the common use of xenografts and collagen membranes, ongoing debate exists regarding their effectiveness [10–12].

To further enhance bone preservation and regeneration, biological adjuncts such as enamel matrix derivatives (EMDs), platelet-derived growth factor, and bone morphogenetic proteins (BMPs) have been introduced in ARP protocols [13, 14]. These biomolecules act as signaling mediators that influence cellular growth, proliferation, migration, and extracellular matrix formation [15]. Integrating such growth factors into ARP treatments may accelerate bone formation and support ridge maintenance [16]. A recent meta-analysis comparing nine ARP modalities to extraction alone showed significant prevention of horizontal bone loss (1.99 mm; 95% CI: 1.54–2.44; $p < 0.00001$), mid-lingual bone height loss (1.99 mm; 95% CI: 0.81–1.52; $p < 0.00001$), and mid-buccal bone height loss (1.72 mm; 95% CI: 0.96–2.48; $p < 0.00001$) [9].

EMDs, derived from developing porcine tooth buds and suspended in a polyglycol gel, are composed predominantly of amelogenin (>95%), along with enamelin and minor proteins [17, 18]. Research indicates that EMDs promote periodontal regeneration by stimulating new cementum formation and exhibit antimicrobial activity against various periodontal pathogens [19–21]. A newer liquid formulation, Osteogain® (Straumann), designed for bone graft combination, demonstrated superior mineralized tissue formation compared with untreated defects in a rabbit guided bone regeneration model [22].

The regenerative capacity of EMDs is attributed to their ability to induce local cytokine production and growth factor release. In vitro studies have shown that EMDs contain TGF-β and BMP-like molecules that activate bone sialoprotein (BSP) gene transcription in osteoblasts through pathways involving fibroblast growth factor (FGF)-2 and TGF-β1 responsive elements [23, 24].

Despite various advancements, no current ARP technique completely prevents ridge contour alteration post-extraction, and no consensus exists regarding the optimal approach for maintaining volumetric, histological, and implant-related parameters. Since EMDs have demonstrated beneficial effects in periodontal regeneration and soft-tissue procedures, their potential application as an adjunct in ARP deserves further exploration. To date, no systematic review has specifically focused on clinical and patient-centered outcomes related to EMD use in ARP.

Experimental findings have revealed that combining EMDs with bovine-derived bone mineral enhances osteoblast adhesion, proliferation, and differentiation [25]. Based on this evidence, the present systematic review was designed to evaluate the effectiveness of EMDs as an adjunctive biomaterial in ARP procedures, with the hypothesis that EMD-enriched xenografts could mitigate alveolar ridge resorption and improve both functional and esthetic outcomes for implant-supported restorations.

Materials and Methods

Search strategy

The present systematic review was designed and executed in alignment with the methodological standards described in the Cochrane Handbook for Systematic Reviews, while the reporting process followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines **(Figure 1)** [26, 27]. Prior to commencing the review, the study protocol was officially recorded in the PROSPERO database (International Prospective Register of Systematic Reviews) under the identification number CRD42021269891 (available at www.crd.york.ac.uk/PROSPERO; accessed on 27 February 2021).

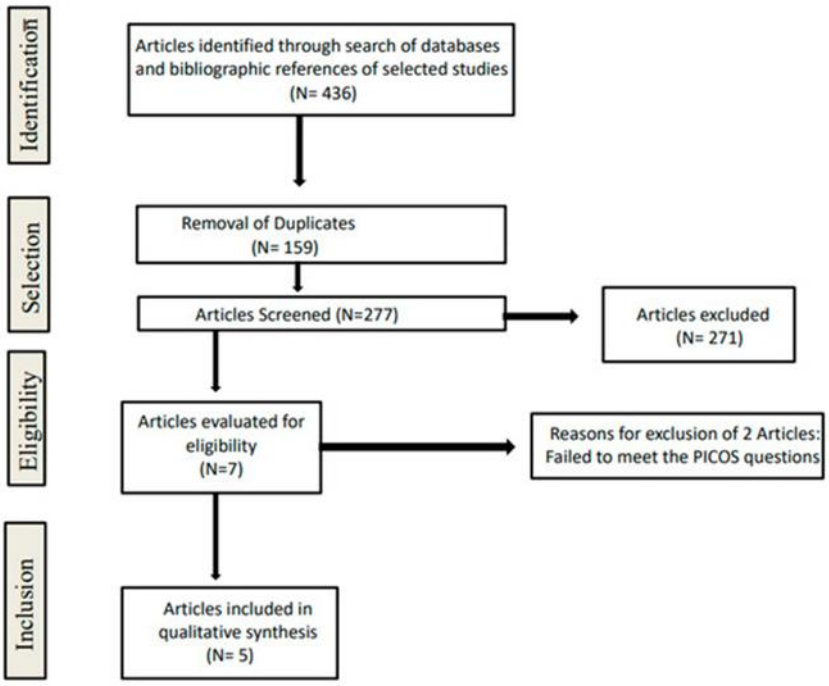

Figure 1. PRISMA flow chart of selection process.

We structured our systematic review protocol to address the specific research question: "In human subjects undergoing tooth or root extraction, what is the additional benefit of incorporating enamel matrix derivatives (EMDs) compared to xenografts alone in alveolar ridge preservation (ARP) procedures?" Accordingly, the PICOS framework was defined as follows: Participants (P) consisted of healthy adults requiring tooth extraction prior to implant placement. The Intervention (I) involved the application of EMDs combined with a xenograft in ARP. The Comparison (C) group included either spontaneous socket healing or ARP performed using a xenograft alone. The Outcomes (O) assessed were histologic, histomorphometric, and radiographic findings, postoperative symptoms, and implant placement feasibility. The Study design (S) was restricted to randomized controlled clinical trials (RCTs) conducted on humans.

Eligibility criteria

Inclusion criteria encompassed only RCTs—either split-mouth or parallel in design—that evaluated the adjunctive effect of EMDs used with xenografts for ARP. Studies were eligible regardless of sample size or follow-up period, provided they analyzed the additional role of EMDs. Exclusion criteria eliminated all non-randomized studies, animal experiments, trials involving immediate implant placement, and publications written in languages other than English.

Data sources and search strategy

A thorough electronic literature search was executed across several databases, including MEDLINE, the Cochrane Library, PsycINFO, Web of Science, Google Scholar, and Scopus. The search was carried out from 10 March to 11 April 2021 without applying restrictions on publication year or language. The primary search formula used was:

((socket [All Fields]) OR (ridge [All Fields])) AND (preservation [All Fields]) AND (enamel matrix derivative [All Fields] OR Emdogain [All Fields] OR amelogenin [All Fields] OR dental enamel proteins [All Fields] OR EMD [All Fields]).

Search terms were refined to suit each database [28]. In addition, manual screening of reference lists from the selected articles and earlier reviews was performed. To ensure inclusivity, clinical trial registries were also consulted, including ClinicalTrials.gov (accessed 15 March 2021), CenterWatch (accessed 20 March 2021), and ClinicalConnection (accessed 22 March 2021).

Study selection and data extraction

Two independent reviewers (O.F. and P.S.) performed the initial screening of titles and abstracts, followed by full-text evaluations of all potentially relevant studies. Any inconsistencies in selection decisions were resolved through discussion. Studies failing to meet the inclusion criteria were excluded, with reasons for exclusion systematically documented. Data extraction was performed using a pretested standardized form, capturing publication year, study location, methodology, patient and tooth characteristics, surgical

details, confounding variables, defect type, follow-up period, and all relevant outcome measures aligned with the study objectives.

Risk of bias assessment

The risk of bias was evaluated independently by the same two reviewers using the Cochrane Collaboration's standardized tool [29]. Six methodological aspects were assessed: sequence generation, allocation concealment, blinding of participants and investigators, blinding of outcome assessors, completeness of outcome data, and selective reporting. Each criterion was rated as low, high, or unclear risk according to Cochrane Handbook guidelines [30]. Any disagreements between reviewers were resolved through consensus discussions.

Results and Discussion

The database search initially retrieved 435 records, and one additional article was identified through manual searching. No unpublished or ongoing trials were included in the review. After duplicate removal, 277 articles underwent title and abstract screening, resulting in seven studies selected for full-text review. Two of these were excluded because their intervention groups did not align with the defined PICO criteria [31, 32]. Ultimately, five studies met all eligibility requirements and were included in this review **(Figure 1)** [33–37]. Due to considerable variability across the studies, a meta-analysis was not possible, and the findings were summarized descriptively.

Risk of bias assessment

Out of the five included studies, three were assessed as having a low risk of bias [34–36], while two were judged as high risk because they did not report on blinding of participants, personnel, or outcome assessors [33, 37]. All studies adequately described sequence generation and allocation concealment. Blinding of participants was reported in two studies [34, 35], whereas only one study described blinding of outcome assessors [36]. The completeness of outcome data and absence of selective reporting were considered acceptable in all studies.

Study characteristics

All five included studies were randomized controlled trials with a parallel-group design, conducted in South Korea, the United States, Australia, and Argentina. No cohort or non-randomized studies fulfilled the inclusion criteria. The primary characteristics and reported outcomes of these studies are presented in **Tables 1 and 2**.

Table 1. Main characteristics of the included studies.

First Author	Year	Study Design	Country	Assessment Techniques	Participant (Teeth) Profile	Confounding Variables 1. Smoking 2. Periodontitis	Defect Features 1. Socket Site 2. Defect Type	Operative Approach 1. Flap Design 2. Soft Tissue Handling 3. Postoperative Antibiotics	Follow-up 1. Observation Duration 2. Withdrawals 3. Complications	Intervention Arms
Nevins [33]	2011	Single-center RCT	USA	Histology (light microscopy, backscatter SEM) Histomorphometry	15 subjects / 16 teeth Age 18–70 years	1. None 2. Not reported	1. Not reported 2. Not reported	1. Full-thickness flap with releasing incisions 2. Not reported 3. Amoxicillin 1.5 g/day × 5 days + 0.12% CHX rinse × 2 weeks	1. 5 months 2. 0 3. No adverse events	T1: DBBMC alone T2: DBBMC + rhPDGF-BB T3: DBBMC + EMD T4: Bone ceramic + EMD
Lee [34]	2019	Single-center RCT	Republic of Korea	Radiography (CBCT) Clinical evaluation Discomfort scoring	32 subjects / 32 teeth 8 males (56.3%), 14 females (43.8%) Mean age 55.1 years (range 31–71)	1. Smokers (>10 cig/day) excluded 2. Stable periodontium (BOP <20%, PI <20%)	1. Maxillary central (n=16) & lateral (n=14) incisors 2. Buccal bone loss ≤50%	1. Flapless / no incision 2. Not reported 3. Amoxicillin 1.5 g/day × 5 days + 0.12% CHX rinse tid × 2 weeks	1. 5 months 2. 2/32 (6.3%) (1 test, 1 control) 3. Bleeding (T=2, C=2); persistent swelling (T=2, C=4); ulceration (T=0, C=1)	Test: DBBMC + EMD + double-layer RCM Control: DBBMC + double-layer RCM

Lee [35]	2020	Single-center RCT	Republic of Korea	Radiography (CBCT) Clinical evaluation Discomfort scoring	36 subjects / 36 teeth 18 males (64.3%), 10 females (35.7%) Mean age 52.9 years (range 22–74)	1. Smokers (>10 cig/day) excluded 2. Stable periodontium (BOP <25%, PI <25%)	1. Maxillary 1st molars (n=21), 2nd molars (n=7) 2. Buccal bone loss ≤50%	1. Flapless / no incision 2. Not reported 3. Amoxicillin 1.5 g/day × 5 days + 0.12% CHX rinse tid × 2 weeks	1. 5 months 2. 8/36 (22.2%) (T1=2, T2=2, C=4) 3. Spontaneous bleeding (p=0.803): T1/T2/C = 9 each; persistent swelling (p=0.661): 9 each; ulceration (p=0.538): 9 each	T1: DBBMC + EMD + double-layer RCM T2: DBBMC + double-layer RCM C: Empty socket
Mercado [36]	2021	Single-center RCT	Australia	Radiography (CBCT) Histology (light microscopy) Histomorphometry	42 subjects / 42 teeth Test: mean age 53.6 ± 10.7 y (66% female) Control: mean age 51.4 ± 11.3 y (71% female)	1. Current smokers excluded 2. Stable periodontium (PD ≤4 mm, BOP <20%, PI <20%)	1. Maxillary anterior teeth 2. Buccal dehiscence ≤1 mm at extraction, no palatal defect	1. Intrasulcular incision (flapless) 2. Free gingival graft 3. 0.12% CHX rinse tid × 1 week, then gel × weeks 2–3	1. 4 months 2. 0 3. No adverse events	Test: DBBMC + EMD Control: DBBMC alone
Bonta [37]	2022	Single-center RCT	Argentina	Histology (light microscopy) Histomorphometry	21 subjects / 21 teeth No further demographic details	1. Not reported 2. Not reported	1. Single anterior sockets 2. Not reported	1. Laterally positioned flap 2. Not reported 3. Not reported	1. 6 months 2. 0 3. Not reported	T1: DBBMC alone T2: DBBMC + EMD C: Empty socket

Abbreviations: T = test; C = control; RCT = randomized controlled trial; FGG = free gingival graft; CHX = chlorhexidine; B-SEM = backscatter scanning electron microscopy; rhPDGF-BB = recombinant human platelet-derived growth factor BB; EMD = enamel matrix derivative; DBBMC = deproteinized bovine bone mineral with 10% collagen; RCM = resorbable collagen membrane; CBCT = cone-beam computed tomography; BOP = bleeding on probing; PI = plaque index; PD = probing depth; tid = three times daily.

Table 2. Measurement Techniques and Findings from the Included Studies

First Author	Histomorphometric Findings	Histologic Findings	First Author	Histomorphometric Findings	Histologic Findings
Nevins 2011 [33]	Proportion of newly formed bone: T1: 28.3 ± 17.2% T2: 39.6 ± 11.3% T3: 23.9 ± 9.3% T4: 21.4 ± 4.2% No significant statistical differences observed	Residual DBBMC particles encased in newly formed and pre-existing bone. Group C findings aligned with those of Group A samples.	**Nevins 2011 [33]**	Proportion of newly formed bone: T1: 28.3 ± 17.2% T2: 39.6 ± 11.3% T3: 23.9 ± 9.3% T4: 21.4 ± 4.2% No significant statistical differences observed	Residual DBBMC particles encased in newly formed and pre-existing bone. Group C findings aligned with those of Group A samples.
Lee 2019 [34]	Not reported	Not reported	**Lee 2019 [34]**	Not reported	Not reported
Lee 2020 [35]	Not reported	Not reported	**Lee 2020 [35]**	Not reported	Not reported

Mercado 2021 [36]	Area fractions of tissue components in core samples: • New bone (NB): T: 45.1 ± 8.8% C: 16.5 ± 6.9% (p < 0.00001) • *Residual graft (RG): T: 20.3 ± 7.2% C: 36.8 ± 8.8% (p < 0.00001)* • Soft tissue matrix (STM): T: 34.6 ± 13.8% C: 46.5 ± 10.4% (p = 0.003)*	Socket filled with NB, RG, and STM in both groups.	**Mercado 2021 [36]**	Area fractions of tissue components in core samples: • New bone (NB): T: 45.1 ± 8.8% C: 16.5 ± 6.9% (p < 0.00001) • *Residual graft (RG): T: 20.3 ± 7.2% C: 36.8 ± 8.8% (p < 0.00001)* • Soft tissue matrix (STM): T: 34.6 ± 13.8% C: 46.5 ± 10.4% (p = 0.003)*	Socket filled with NB, RG, and STM in both groups.
Bonta 2022 [37]	New bone (NB): (p < 0.05) *T1: 47.30% T2: 32.27% C: 35.62% Residual graft (RG): (p > 0.05) T1: 11.61% T2: 18.12% Soft tissue matrix (STM): (p < 0.05)* T1: 57.21% T2: 34.57% C: 64.38%	Healthy lamellar bone with osteons present in all groups; no inflammatory cells in marrow spaces. DBBMC remnants surrounded by new and native bone in T1 and T2.	**Bonta 2022 [37]**	New bone (NB): (p < 0.05) *T1: 47.30% T2: 32.27% C: 35.62% Residual graft (RG): (p > 0.05) T1: 11.61% T2: 18.12% Soft tissue matrix (STM): (p < 0.05)* T1: 57.21% T2: 34.57% C: 64.38%	Healthy lamellar bone with osteons present in all groups; no inflammatory cells in marrow spaces. DBBMC remnants surrounded by new and native bone in T1 and T2.

T: test group; C: control group; OSFE/BAOSFE: osteotome sinus floor elevation or bone-added OSFE; SFEL: lateral-approach sinus floor elevation; RW: ridge width; BH: buccal height; PH: palatal height; NB: new bone; RG: residual graft; STM: soft tissue matrix; BT: buccal bone thickness; *: statistically significant difference between test and control groups.

Confounding variables such as systemic conditions, medication use, periodontitis, and smoking were infrequently documented across the studies. The location of extraction sites varied: two studies focused solely on maxillary anterior teeth [34, 36], one investigated first and second molar sockets [35], another did not specify tooth location [33], and one included single anterior extractions [37]. The morphology of the defects at extraction ranged from 50% buccal bone loss to ≤1 mm buccal dehiscence **(Table 1)**.

Intervention details

All studies employed a combination of enamel matrix derivatives (EMDs) with deproteinized bovine bone mineral containing 10% collagen (DBBMC, Geistlich Bio-Oss®, Wolhusen, Switzerland) as the graft material. In two trials, both experimental and control sites were covered with a bilayer, non-cross-linked resorbable collagen membrane [34, 35], whereas the other studies left the sockets uncovered [33, 36, 37]. Surgical approaches differed: two studies used a flapless technique [34, 35], one elevated full-thickness flaps with vertical incisions [33], another performed intrasulcular incisions without flap elevation [36], and the most recent study raised only a lingual or palatal flap to achieve primary closure without manipulating the vestibular flap [37].

Postoperative care also varied: three studies administered amoxicillin 1.5 g/day for five days along with a 0.12% chlorhexidine mouth rinse for two weeks [33–35], while one study used a 0.12% CHX rinse for one week followed by CHX gel in weeks two and three [36]. Follow-up duration ranged from three months in three studies, four months in one, to six months in the latest study **(Table 1)**.

Radiographic findings

Three studies assessed horizontal and vertical bone dimensions using CBCT at baseline and after four or five months [34–36]. None of these studies reported significant differences between the EMD + DBBMC and control groups in terms of horizontal or vertical bone changes.

Histologic and histomorphometric findings

Histologic analyses were performed in three studies [33, 36, 37]. One study found no significant differences between groups in new bone formation or tissue composition [33]. The other two studies quantified tissue fractions—new bone (NB), residual graft (RG), and soft tissue/marrow spaces (STM)—at magnifications up to 40× [36, 37]. One study reported that sockets treated with DBBMC + EMD had 45.1 ± 8.8% new bone, which was significantly higher than 16.5 ± 6.9% in the DBBMC-only group (p < 0.00001).

Residual graft percentages were greater in controls (36.8 ± 8.8%) than in the test group (20.3 ± 7.2%, $p < 0.00001$), and STM content was also higher in controls (46.5 ± 10.4%) compared to the test group (34.6 ± 13.8%, $p < 0.003$).

Postoperative symptoms

Two studies evaluated postoperative discomfort [34, 35]. One study reported no differences in pain severity, swelling, or duration between groups [35], while the other found that the DBBMC + EMD group experienced a shorter duration of pain and swelling, although intensity was similar between groups [34].

Implant placement feasibility

Three studies assessed implant placement after ARP [33, 35, 36]. All demonstrated successful implant insertion with no significant differences between the EMD-treated and control groups **(Table 2)**.

In recent years, numerous surgical strategies have been proposed to maintain alveolar ridge dimensions following tooth extraction [9, 38, 39]. This systematic review aimed to collate and critically assess the available evidence regarding the use of enamel matrix derivatives (EMDs) in alveolar ridge preservation (ARP).

Extraction sockets are typically self-contained, which may limit the additional benefits of adjunctive materials beyond conventional bone grafts for space maintenance or collagen membranes for soft tissue exclusion [38]. This, however, does not imply that these agents are ineffective; rather, it reflects the absence of standardized application protocols [39]. Consistent with this perspective, several studies have reported potential advantages of incorporating bioactive agents, such as platelet-rich fibrin (PRF) and recombinant human bone morphogenetic protein-2 (rhBMP-2), in ARP procedures [14, 39–43]. For example, in a clinical trial assessing rhBMP-2 in extraction sockets with over 50% buccal dehiscence, CBCT analyses demonstrated partial buccal bone regeneration compared to a collagen carrier alone, and implant placement was feasible at five months. The test group showed statistically significant improvements in clinical ridge width (6.0 vs. 4.62 mm), radiographic ridge width (6.17 vs. 4.48 mm), and buccal plate regeneration (4.75 vs. 1.85 mm; $p < 0.05$) [40].

Another split-mouth RCT evaluated dimensional changes and bone formation using leucocyte- and platelet-rich fibrin (L-PRF) or advanced platelet-rich fibrin+ (A-PRF+) compared to natural healing [41]. Although buccal and palatal ridge changes at 1 mm below the crest were not statistically different ($p > 0.05$), socket fill was higher in the L-PRF (85.2%) and A-PRF+ (83.8%) groups compared to controls (67.9%). Radiographic and histologic analyses further confirmed greater new bone formation in PRF-treated sites, with no significant difference between L-PRF and A-PRF+ groups.

Despite these findings, systematic reviews consistently highlight the limited high-quality evidence regarding bioactive materials in ARP. Additional well-designed RCTs and long-term studies are required to clarify the benefits and limitations of PRF, rhBMP-2, and other biologics in ridge preservation [42]. The variability in adjunctive materials and study designs complicates direct comparisons, including those involving EMDs.

Currently, only a small number of RCTs have investigated the adjunctive effect of EMDs in ARP, exhibiting substantial heterogeneity in study design and extraction sites. The most recent guidance from the American Academy of Periodontology evaluated only two studies on EMDs in ARP [34, 36]. In contrast, this review incorporates these studies along with three additional trials, representing the first systematic review dedicated exclusively to EMD application in ARP.

Preclinical studies have demonstrated the osteogenic potential of EMDs in both in vitro and in vivo models [16, 44, 45]. In vivo data indicate that EMDs can upregulate osteogenic gene expression in progenitor cells [46–49], while also inhibiting bone resorption through increased osteoprotegerin (OPG) and reduced receptor activator of nuclear factor kappa B ligand (RANKL) expression [50–52]. Additionally, EMDs promote proliferation and differentiation of bone cells [18, 53] and enhance the osteogenic capacity of bone marrow, leading to increased mineralized nodule formation [54].

In three studies included in this review, histomorphometric analysis of core samples collected during implant placement was performed to evaluate tissue composition [33, 36, 37]. One of these studies found no notable differences in new bone formation [33], but it provided limited information on socket sites and defect characteristics, and each group included only four teeth, reducing the reliability and generalizability of the results [33]. Conversely, two studies with larger sample sizes (21 teeth per group) reported significant differences between test and control sites in the proportions of new bone, residual graft material, soft tissue, and marrow spaces [36, 37]. The observed increase in new bone in test groups suggests that EMD application enhances bone regeneration, consistent with previous findings. EMDs have also been associated with upregulation of vascular endothelial growth factor (VEGF), which promotes

angiogenesis and improved blood supply, potentially supporting bone formation within extraction sockets [46, 55, 56].

Patient-reported outcomes (PROs) were assessed in two studies from the same research group [34, 35]. In a study involving maxillary incisors, patients in the EMD-treated group experienced shorter durations of pain and swelling [34]. However, in a study on maxillary molars, no differences in postoperative discomfort were observed between groups [35]. These results indicate that EMDs may help alleviate postoperative discomfort in some cases, but the limited evidence prevents firm conclusions, emphasizing the need for further trials. The biological mechanisms behind EMDs' effects in extraction sockets and surgical wounds are not fully clarified, although they are believed to promote early wound healing by enhancing angiogenesis, stimulating TGF-β1 production, and increasing proliferation and migration of microvascular endothelial cells [57–61].

Given the small number of studies included, these findings should be interpreted with caution. Quantitative synthesis was not feasible due to heterogeneity in clinical measures. Nonetheless, qualitative analysis of radiographic, histomorphometric, and patient-reported outcomes generally favored the test groups, although statistical significance was not consistently achieved, and the evidence is based on a limited number of reports.

Conclusion

Based on the qualitative evidence available, EMDs may contribute to faster resolution of postoperative discomfort and improved new bone formation, although the impact on ridge dimensions and radiographic outcomes remains unclear. Further multicenter studies with standardized methods are necessary to better define the potential benefits of EMDs in alveolar ridge preservation following tooth extraction.

Acknowledgments: None

Conflict of Interest: None

Financial Support: None

Ethics Statement: None

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