



## Coronally advanced flap surgery with enamel matrix derivative in the treatment of gingival recession: a systematic review

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### ABSTRACT

**Objective:** Based on a review of the literature, we evaluated the clinical effect of the combination of enamel matrix derivative proteins (EMDP) and coronally advanced flap (CAF) surgery in the treatment of gingival recession (GR).

**Methods:** Information was retrieved from the electronic databases PubMed, Lilacs, Scielo, Medline and the Cochrane Library. Controlled, randomized clinical studies of intervention in humans published in English or Spanish between 2000 and 2013 were eligible.

**Results:** The initial sample consisted of 171 publications. Of these, eight were selected which compared CAF+EMDP (study) with CAF alone (control) in the treatment of GR. Invariably, RH decreased in both the study group and the control group. Likewise, GR width and probing depth decreased and the clinical attachment level increased in both groups, but results were significantly better in the study group.

**Conclusion:** Despite the absence of an overall significant difference between treatment with CAF + EMDP and CAF alone, the addition of EMDP appears to increase the likelihood of achieving complete root coverage and clinically and aesthetically satisfactory results.

**Key words:** Gingival recession; Enamel matrix derivative; Coronally advanced flap

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### Retalho posicionado coronariamente associado à proteína derivada da matriz do esmalte no tratamento de recessões gengivais: revisão sistematizada da literatura

#### RESUMO

**Objetivo:** Este estudo avaliou por meio de uma revisão da literatura, o efeito clínico do retalho posicionado coronariamente (RPC) associado a proteínas derivadas da matriz do esmalte (PDME) no tratamento das recessões gengivais (RG).

**Metodologia:** Foram consultadas bases de dados eletrônicas: PubMed, Lilacs, Scielo, Medline e o Centro de Registro de Ensaios Clínicos Controlados e incluídos estudos clínicos de intervenção em humanos, randomizados, controlados, publicados em língua inglesa ou espanhola, entre 2000 e 2013.

**Resultados:** Foram encontradas 171 referências e com a análise dos títulos e resumos, oito estudos que abordaram aplicação de PDME em associação com o RPC para o tratamento de RG, que utilizavam no grupo controle apenas RPC, fizeram parte desta revisão. Esses trabalhos relataram uma redução significativa na altura das RG tratadas com RPC e RPC+PDME. Houve redução da largura da RG e profundidade de sondagem, com ganhos no nível de inserção clínica em ambos os tratamentos, com melhores resultados no grupo RPC + PDME.

**Conclusões:** Apesar de não existirem diferenças significativas em um aspecto geral na cobertura radicular com o uso do RPC isolado ou combinado com PDME, esta combinação pode favorecer o recobrimento radicular completo ou melhorar os níveis de recobrimento radicular.

**Palavras-chave:** Recessão gengival; Proteína derivada da matriz do esmalte; Retalho posicionado coronalmente

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## INTRODUCTION

Gingival recession (GR) occurs when the gingival margin is apical to the cemento-enamel junction, clinically resulting in exposure of the root surface and loss of attachment [1]. The etiology of GR involves a wide range of factors, including periodontal disease, excessive tooth-brushing force, iatrogenesis (orthodontic tooth movement, defective fillings) and anatomical conditions (mal-positioned teeth, muscle attachment, abnormal frenum attachment) [2]. GR affects populations regardless of their standards of oral hygiene [3]. Associated with pain and dental tenderness, the condition can compromise aesthetics and dental vitality [4]. It is also an important risk factor for the development of root caries [4,5].

GR may be classified according to severity based on the prognosis of root coverage with mucogingival surgical procedures [6]. Thus, patients with Miller's class I and II GR present no periodontal attachment loss in the interproximal area and complete root coverage is achievable. In Miller's class III GR, loss of periodontal attachment is mild to moderate and only partial root coverage is achievable. Finally, in Miller's class IV GR, interproximal tissue loss is so severe that no root coverage is possible [6].

The choice of surgical technique for root coverage in GR depends mainly on patient demands and on local anatomical characteristics, such as recession height and width, interdental soft tissue dimensions, recessions in adjacent teeth, root caries and cervical abrasions [7].

A range of plastic surgery procedures have been proposed for the treatment of GR, including free gingival graft (FGG), connective tissue graft (CTG), guided tissue regeneration (GTR) and pedicled flaps (PF) [8].

One of the most widely used surgical techniques of root coverage is coronally advanced flap (CAF) [9]. When this technique is used in patients with Miller's class I and II GR, the average root coverage achieved is between 64% [10] and 99% [11], and the aesthetic results are generally excellent, with no need for a second surgical site. The procedure is simple to perform and may be used to treat multiple recessions as well [12].

Several clinical studies have explored the combination of enamel matrix derivative proteins (EMDP) and surgical root coverage procedures (especially CAF) in order to improve root coverage predictability and periodontal regeneration of the previously exposed root surface [13-18]. Histological analyses of bone defects treated with EMDP show the formation of a new acellular extrinsic fiber cementum attached to the underlying dentin. In addition, a new periodontal ligament, including the attachment of functionally oriented collagen fibers and alveolar bone, may be observed [19].

The purpose of the present study was to compare the clinical effect of CAF with and without EMDP in the treatment of gingival recession, based on a review of the literature.

## METHODOLOGY

The review of the literature was based on a search in electronic databases, including PubMed, Lilacs, Scielo, Medline and the Cochrane Library, using the following descriptors: coronally advanced flap, enamel matrix proteins, root coverage and gingival recession. The search was narrowed by selecting only controlled, randomized clinical studies of intervention in humans published in English or Spanish between 2000 and 2013. The initial sample consisted of 171 abstracts. After analyzing the titles and abstracts, the complete texts were retrieved and screened using the following criteria:

- blind or double-blind study,
- type of intervention: use of combination of EMDP and CAF in the treatment of single or multiple GR,
- control group: GR treated with CAF alone.

To minimize the risk of bias, the selected articles were analyzed by two independent reviewers (Y.L.B. and V.R.S.S.). Discrepancies regarding the eligibility of articles were discussed extensively by the reviewers. When an agreement could not be reached, a third investigator (M.M.S.M.M.) was consulted. The final sample consisted of 8 publications.

## RESULTS

Table 1 shows in chronological order the main characteristics of clinical studies comparing the clinical effect of CAF with and without EMDP in the treatment of gingival recession [20-27].

The following eight publications were included in the final analysis: Modica et al. [20], Hägewald et al. [21], Cueva et al. [22], Del Pizzo et al. [23], Spahr et al. [24], Castellanos et al. [25], Piloni et al. [26] and Cordaro et al. [27]. The study by Cueva et al. [22], included patients with Miller's class III GR, but the number of patients in this category was not specified.

The seven most important clinical parameters evaluated in these articles were: recession height (RH), recession width (RW), probing depth (PD), clinical attachment level (CAL), keratinized tissue width (KT), alveolar bone level (ABL) and percentage root coverage (RC). However, not all the studies in the sample evaluated all seven parameters.

### Recession height (RH)

This parameter was evaluated in all the studies. Invariably, RH decreased in both the study group (CAF + EMDP) and the control group (CAF) but the reduction was greater in the former [20-17]. However, the difference in RH between the study group and the control group was only statistically significant in three studies: Cueva et al. [22] – reduction from 2.77±0.62 mm to 0.19±0.15 mm versus from 2.68±0.65 mm to 0.77±0.25 mm ( $p<0.001$ ); Castellanos et al. [25] – reduction from 2.68±1.63 mm to 0.36±0.60 mm versus from 2.31±1.52 to 0.90±0.95 mm ( $p<0.05$ ); and Piloni et al. [26] – reduction from 2.86±0.64 mm to 0.13±0.06 mm versus from 2.66±0.70 mm to 1.53±0.50 mm ( $p<0.001$ ).

**Table 1.** Summary of the eight studies included in the present systematic review evaluating the clinical effect of coronally repositioned flap (CAF) surgery, alone or in combination with enamel matrix derivative proteins (EMDP), in the treatment of gingival recession. Continued Table 1.

| Study (year)                   | Methods  | Participants   | Intervention   | Evaluated clinical parameters | Type of recession treated*  | Blinded investigator | Main findings  |
|--------------------------------|--|--|--|-------------------------------|---|----------------------|--|
| Modica et al. (2000) [20]      | Controlled randomized clinical trial, split-mouth design, 2 groups, 6 months.          | 12 subjects (7 men / 5 women).<br>Average age: 33.8 years.<br>Non-smokers.                               | Control group: CAF (14 treated sites).<br>Study group: CAF+EMDP (14 treated sites).                                      | RH, PD, CAL, KT.              | I and II (20 isolated defects with RH $\geq$ 3 mm, and 8 multiple effects with RH $\geq$ 3 mm). | Yes.                 | After 6 months, a significant intragroup difference was observed with regard to CAL. However, no significant intergroup difference was observed with regard to any parameter (RH, PD, CAL and KT).   |
| Hägeward et al. (2002) [21]    | Placebo-controlled randomized clinical trial, split-mouth design, 2 groups, 12 months. | 36 subjects (19 men / 17 women)<br>Average age: 36 years.<br>Non-smokers                                 | Control group: CAF+ placebo (propylene glycol alginate) (36 treated sites).<br>Study group: CAF+EMDP (36 treated sites). | RH, RW, PD, CAL, KT, ABL.     | I and II (72 isolated defects with RH $\geq$ 3 mm).   | Yes.                 | After 12 months, both groups had experienced a similar increase in CAL. Changes in KT were significantly greater in the study group ( $p=0.003$ ). No significant difference was observed for any other parameter (RH, RW, PD, CAL and ABL). |
| Cueva et al. (2004) [22]       | Controlled randomized clinical trial, split-mouth design, 2 groups, 6 months.          | 17 subjects (6 men / 11 women).<br>Average age: 39 years.<br>2 smokers                                   | Control group: CAF (29 treated sites).<br>Study group: CAF+EMDP (29 treated sites).                                      | RH, RW, PD, CAL, RC, KT.      | I, II and III (20 isolated defects with RH $>$ 2 mm, and 38 multiple effects with RH $>$ 2 mm). | Yes.                 | After 6 months, the study group presented significantly smaller RH and RW values and significantly greater RC ( $p<0.001$ ) and KT ( $p<0.005$ ) values.   |
| Del Pizzo et al. (2005) [23]   | Placebo-controlled randomized clinical trial, split-mouth design, 2 groups, 24 months. | 15 subjects (4 men/11 women).<br>Average age: 39.46 years.<br>Non-smokers.                               | Control group: CAF+ placebo (propylene glycol alginate) (15 treated sites).<br>Study group: CAF+EMDP (15 treated sites). | RH, RW, PD, CAL, KT.          | I and II (30 isolated defects with RH $\geq$ 3 mm).   | Yes.                 | After 24 months, no significant intergroup difference was found for the parameters RH, RW, PD, CAL and KT, but significant intragroup differences were observed for RH and LAC.  |
| Spahr et al. (2005) [24]       | Controlled randomized clinical trial, split-mouth design, 2 groups, 24 months.         | 30 subjects (18 men/12 women).<br>Average age: 36.5 years.<br>5 smokers (<10 cigarettes per day).        | Control group: CAF (30 treated sites).<br>Study group: CAF+EMDP (30 treated sites).                                      | RH, RW, PD, CAL, KT, ABL.     | I and II (60 isolated defects with RH $\geq$ 3 mm).   | Yes.                 | After 24 months, the groups did not differ significantly with regard to RH, KT, CAL or ABL. However, PD ( $p=0.0463$ ) and RW ( $p=0.0274$ ) improved significantly in the study group.  |
| Castellanos et al. (2006) [25] | Controlled randomized clinical trial, parallel design, 2 groups, 12 months.            | 22 subjects (9 men/13 women).<br>Average age: 42.5 years.<br>Non-smokers.                                | Control group: CAF (11 treated sites).<br>Study group: CAF+EMDP (11 treated sites).                                      | RH, RW, PD, CAL, KT.          | I and II (22 isolated defects with RH $>$ 2 mm).  | Not specified.       | After 12 months, RH and RW values were significantly higher in the study group. In both groups, the increase in RC, CAL and KT was significant. The groups did not differ significantly with regard to PD and CAL.                           |
| Pilloni et al. (2006) [26]     | Controlled randomized clinical trial, parallel design, 2 groups, 18 months.            | 30 subjects (17 men/13 women).<br>Age range: 19-67 years.<br>Non-smokers.                                | Control group: CAF (15 treated sites).<br>Study group: CAF+EMDP (15 treated sites).                                      | RH, PD, CAL, KT.              | I and II (30 isolated and multiple defects, minimum size not specified).                        | Yes.                 | After 18 months, the groups did not differ significantly with regard to PD, but RH ( $p<0.01$ ), CAL ( $p<0.001$ ) and KT ( $p<0.05$ ) improved significantly in the study group compared to the control group.                              |
| Cordaro et al. (2012) [27]     | Controlled randomized clinical trial, split-mouth design, 2 groups, 24 months.         | 10 subjects (gender ratio not specified).<br>Age range: 18-60 years.<br>Number of smokers not specified. | Control group: CAF (29 treated sites).<br>Study group: CAF+EMDP (29 treated sites).                                      | RH, PD, CAL, KT.              | I and II (58 multiple defects with RH $\geq$ 2 mm).   | Yes.                 | After 24 months, no significant differences were observed between the groups with regard to any parameter (RH, PD, CAL and KT).  |

RH = recession height; RW = recession width; PD = probing depth; CAL = clinical attachment level; KT = keratinized tissue width; ABL = alveolar bone level; RC = percentage root coverage; CAF = coronally advanced flap; PDME = enamel matrix derivative proteins.

\* Based on Miller's classification (1985).

## Recession width (RW)

This parameter was not evaluated in three studies [20, 26,27]. As for the other five studies, RW decreased in both the study group (CAF+EMDP) and the control group (CAF) but the reduction was invariably greater in the former. However, the difference in RH between the study group and the control group was only statistically significant in three studies [22,24,25]: reduction from 3.92±0.36 mm to 0.80±0.50 mm versus from 3.80±0.30 to 2.11±0.50 mm ( $p<0.001$ ) [22]; reduction from 4.33±0.77 mm to 2.88±1.61 mm versus from 4.42±0.81 mm to 1.95±1.72 mm ( $p=0.0274$ ) [24]; reduction from 4.27±2.06 mm to 0.77±0.87 mm versus from 3.68±1.91 mm to 1.72±1.31 mm ( $p=0.025$ ) [25].

## Probing depth (PD)

This parameter was evaluated in all the studies. In seven studies [20-22,24-27], PD decreased in both the study group (CAF+EMDP) and the control group (CAF). The study by Del Pizzo et al. [23], was the only to report similar PD values regardless of treatment (group) and time (24 months). The difference in PD between the study group and the control group was statistically significant in only one study: reduction from 1.76±0.61 mm to 0.66±0.68 mm (study group) versus from 1.58±0.65 mm to 0.32±0.83 mm (control group) ( $p=0.0463$ ) [24].

## Clinical attachment level (CAL)

This parameter was evaluated in all the studies. Invariably, CAL decreased in both the study group (CAF+EMDP) and the control group (CAF) but the reduction was greater in the former [20-27].

The difference in CAL between the study group and the control group was statistically significant in only one study [26]: reduction from 3.80±0.67 mm to 1.00±0.00 mm versus from 3.60±0.70 mm to 1.53±0.50 mm ( $p<0.001$ ).

## Keratinized tissue width (KT)

This parameter was evaluated in all the studies. In one study [26], KT decreased in the control group (CAF). In the other seven studies, KT increased in both the study group (CAF+EMDP) and the control group (CAF) but the increase was invariably greater in the former. However, the difference in KT between the study group and the control group was only statistically significant in three studies [21,22,26]: increase from 2.10±1.00 mm to 2.80±0.90 mm versus from 2.40±1.00 mm to 2.70±0.9 mm ( $p=0.003$ ) [21]; increase from 2.04±0.55 mm to 2.64±0.28 mm versus from 2.14±0.43 mm to 2.09±0.24 mm ( $p=0.005$ ) [22]; increase from 1.80±0.75 to 1.93±0.50 mm versus from 1.66±0.60 mm to 1.46±0.60 mm ( $p<0.05$ ) [26].

## Alveolar bone level (ABL)

This parameter was evaluated in only two studies [21, 24]. In both of these, ABL increased significantly after the treatment, but the groups did not differ significantly.

## Percentage root coverage (RC)

The highest RC value (93.8±12.9%) was that of the study group in Pilloni et al. [26], with complete coverage in 13 of 15 treated sites. The lowest RC value (62.2%) was that of the control group in Castellanos et al. [25], with complete coverage in only 4 of 11 treated sites. In another study [22], 7 sites were initially identified as Miller's class III GR; of these, three were treated with EMDP, while four were controls. Complete coverage was achieved for two recessions in the former group and for one recession in the latter group.

## Histological findings

Only one study provided histological information [25]: gingival tissue on the buccal side treated with EMDP was evaluated microscopically following the removal of a tooth for orthodontic purposes. The margin of the junctional epithelium was coronal to the treated recession, as indicated by the level of root instrumentation, and regenerating supportive periodontal tissues were observed coronally to this area.

## DISCUSSION

A range of techniques have been developed to achieve complete root coverage in patients with GR. In addition, modifications made over the years have improved the predictability of these procedures. In the past, FGG was widely used, with different levels of success [28,29]. Today, CTG, originally introduced by Langer and Langer [30] and CAF [31,32], or a combination of these two techniques [33-35], are among the most popular procedures, with greatly improved predictability.

CTG is associated with high success rates and excellent aesthetic results in the short and long run when used in patients with Miller's class I and II GR. It is also used as a standard to evaluate other techniques of root coverage [36]. In fact, the percentage root coverage has been shown to be similar for recessions treated with CAF+EMDP and with CAF+CTG. According to the authors, the only advantage of adding CTG to the treatment was an increase in KT [18,37]. In all the studies reviewed for this paper, KT values were higher in groups treated with CAF + EMDP than in groups treated with CAF alone, and in three studies the difference was significant [21,22,26].

Thus, it may be concluded that, on the average, similar root coverage may be achieved with either combination (CAF+EMDP vs. CAF+CTG). However, since no second surgical site is needed with the combination CAF+EMDP, the procedure is associated with less postoperative discomfort [18]. In a study on dogs with induced GR treated surgically with either CAF or CAF + EMDP, histometrical analyses showed the two options to be similar with regard to root coverage and tissue repair [38].

Despite variations in results, microscopic analyses revealed newly formed cementum, with attachment of

connective tissue fibers and islands of bone tissue in roots treated with EMDP [39,40]. These findings match the results of the only study included in the present review which reported periodontal regeneration in tissue analyzed histologically [25].

The role of EMDP in periodontal regeneration was demonstrated in experimental recessions by Heijl [41]. In that study, the new cementum was observed histologically to cover 73% of the initial defect, while ABL increased by 65%.

The mechanism of EMDP-induced periodontal regeneration appears to involve periodontal ligament cells [42]. EMDP, of which amelogenins constitute a major component [43], seem to mimic the embryonic phases of odontogenesis mainly by promoting the formation of a cementum-like mineralized tissue which may serve as a matrix for repopulation with periodontal ligament cells [44,45].

In patients with high aesthetic expectations, CAF is the procedure of choice, provided enough keratinized tissue is present apically to the exposed root [7,46]. The soft tissue used to cover the recession is similar to the original tissue with regard to color, texture and thickness, leading to satisfactory aesthetic results [47].

In a case series evaluated by Abbas et al. [17], the combination CAF+EMDP was found to be a predictable procedure in the correction of GR defects, with excellent results in terms of root coverage and clinical attachment. In the eight studies reviewed here, 100% root coverage was achieved for a total of 81 sites treated with CAF+EMDP, as opposed to 47 sites treated with CAF only. In addition, in all treated recessions CAL increased and RH and RW decreased, especially in the study group (CAF+EMDP). A systematic review and meta-analysis [48] of the use of EMDP in periodontal therapy found that the combination CAF+EMDP was significantly more efficient than CAF alone with regard to root coverage (odds ratio: 3.5).

The authors of this review subscribe to the view that CAF is a safe and reliable periodontal plastic surgery procedure capable of reducing gingival recession and, in many cases, achieve complete root coverage. In the reviewed articles, the addition of EMDP produced similar results in terms of root coverage. Small, non-significant clinical differences in favor of the combination CAF+EMDP were found. In other systematic reviews [48,49], the addition of EMDP improved root coverage outcomes.

The present review was limited by the short follow-up time of each study, by the lack of sample calculation and by the method of evaluation of clinical parameters.

## CONCLUSION

The application of enamel matrix derivative proteins can improve the clinical outcome of surgical correction of gingival recession with coronally advanced flap technique, especially with regard to root coverage, keratinized tissue width and recession size. Thus, despite the absence of an overall significant difference between treatment with

CAF+EMDP and with CAF alone, the addition of EMDP increases the likelihood of achieving complete root coverage and clinically and aesthetically satisfactory results.

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