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Efficacy of Root Surface Biomodification in Root Coverage: A Systematic Review

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Abstract

Background: Although many authors have reported the use of root surface biomodification (RSB), the clinical outcomes in terms of root coverage are still unclear, as a number of biomodifier agents have been used in combination with various periodontal plastic surgical techniques. In this review we aim to evaluate the efficacy of RSB in root coverage and its impact on the outcomes.

Methods: A search of MEDLINE and Cochrane databases was carried out along with 2 manual searches. A combination of specific terms was used to identify relevant studies that met well-defined inclusion and exclusion criteria. Clinical attachment level, probing depth and percentage root coverage after treatment were among the results expected to be reported in the included articles.

Results: A total of 10 articles were identified and data were extracted. Only 6 met the inclusion criteria. Among these 6 studies, citric acid, ethylenediaminetetraacetic acid and laser therapy were used as RSB agents and free gingival graft, subepithelial connective tissue graft plus coronally advanced flap and semilunar coronally repositioned flap were the surgical approaches to root coverage treatment. Baseline and outcome data were analyzed and compared.

Conclusion: RSB provided no additional benefit in terms of the evaluated clinical parameters. Within the limitations of this review, we found no evidence to support the use of RSB prior to root coverage treatment.

A significant proportion of the adult population is affected by this alteration,²⁻⁴ which may lead to esthetic concerns and complaints of hypersensitivity.⁵ Local trauma, anatomic factors and inflammatory conditions are the main causes of gingival recession.^{6,7}

Several surgical approaches can be used to achieve root coverage. Laterally^{8,9} and coronally advanced flaps,¹⁰ free^{11,12} and subepithelial connective tissue grafts,¹³ guided tissue regeneration¹⁴ and combined techniques with variants¹⁵ have resulted in various rates of success. Regardless of technique, the ultimate goal is complete root coverage, and attempts have been made to increase the success rate and predictability of various techniques.^{16,17}

Some authors suggest that root surface biomodification (RSB) with chemical agents, in conjunction with scaling and root planing, improves gingival attachment.¹⁸ These agents remove the smear layer, exposing collagen fibres on the dentin matrix and eliminating cytopathic substances that inhibit human gingival fibroblast growth.¹⁹ Citric acid,^{8,9,11,12,20} tetracy-

Gingival recession is characterized by displacement of the gingival margin apically from the cemento-enamel junction resulting in root surface exposure.¹

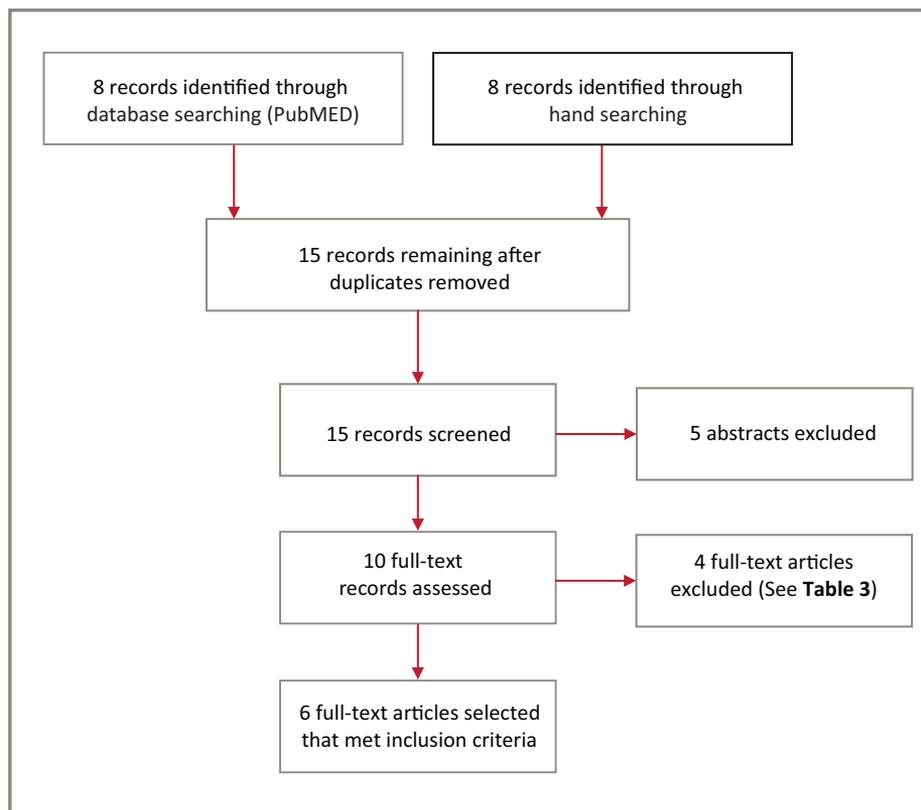


Figure 1: Search strategy used to identify articles for review.

publications; and interpretation of the evidence found in the literature retrieved.

Material and Methods

Literature Search

The search for relevant studies to be included in this review was carried out in 3 steps.

On 30 March 2011, MEDLINE was searched for entries since 1 January 1966. The search was limited to randomized controlled trials, published in English, in humans over 19 years of age, with an available abstract (**Table 1**). On the same day, the Cochrane Central Register of Controlled Trials was consulted using the following strategy: “Gingival recession” [search all text] AND “Root coverage” [search all text]. Articles appearing in both database searches were considered only once. To ensure the widest possible search, the indexing terms were used as both MeSH

cline,¹³ sodium hypochlorite⁹ and ethylenediaminetetraacetic acid (EDTA)^{21,22} are the main substances used; more recently, lasers^{23,24} have also been employed.

Despite the variety of agents, reviews have not shown a significant improvement in root coverage with the use of RSB.^{17,25,26} However, such studies have compared specific biomodifier agents and a limited number of techniques; none has compared surgical approaches with various RSB protocols. In addition, although these reviews have suggested that RSB is irrelevant, none had RSB assessment as a primary objective.

This study aimed to review the literature systematically to answer the question: does RSB have any positive or negative effect when used before root coverage procedures? We followed the approach outlined in the Cochrane Collaboration’s Handbook²⁷: specification of the problem (see above); formulation of a plan to conduct a literature search using specific index terms and retrieve

terms and free text in the MEDLINE search, and the truncation symbol * was used in the Cochrane Library search.

To identify studies not found in the databases search, issues of the following journals, published between January 2000 and December 2010, were searched manually: *Journal of Periodontology*, *Journal of Clinical Periodontology*, *International Journal of Periodontics and Restorative Dentistry* and *Journal of Periodontal Research*.

In addition, the reference lists of the studies identified in the online and manual searches described above were also checked. During this search, an effort was made to identify titles containing words suggesting root coverage approaches, such as coronally or laterally repositioned flaps, semilunar coronally repositioned flap, subepithelial connective tissue graft and other surgical techniques; and words suggesting an RSB technique, such as EDTA, citric acid and tetracycline.

Abstracts or unpublished studies were not included. (The literature search is summarized in Fig. 1).

Selection criteria

To be included in this review, the study had to meet the following criteria, which were considered during all 3 steps of the search.

- *Inclusion criteria:* Randomized controlled trials in systemically healthy human nonsmokers; patients with Miller’s class I or II gingival recession or deeper than 3 mm but without interdental bone loss; published in English; presenting any modality of RSB in the test group; and including baseline data and final measurements of recession.
- *Exclusion criteria:* Studies in animals; lacking baseline–outcome comparisons; with insufficient data; with more than one variable in addition to RSB; and case reports, book chapters and narrative reviews because of their weaker clinical evidence.

Study Analysis and Data Extraction

Abstracts of the selected articles were read by both authors independently. The full text was ordered for all studies appearing to meet the inclusion criteria, for studies for which an abstract was considered relevant by at least 1 author and when the title, keywords and abstract contained insufficient information to make a decision.

Reading of relevant studies and quality evaluation²⁸ were carried out independently by both authors to assess their suitability for this review. A study was considered good when it met all the criteria and fair when it did not meet all criteria but was judged to have no fatal flaw that would invalidate its results.²⁸ Disagreements between the authors were resolved through discussion of the study’s design and characteristics to reach a consensus on inclusion or exclusion. Articles were excluded if agreement could not be reached.

Data from the included articles were extracted with the aid of a protocol sheet designed especially for this study. They included assessment of variables, such as the extent of recession before and after surgery, probe depth, root sensitivity, percentage of coverage and increase in keratinized mucosa.

Table 1 Search strategy and number of publications retrieved from MEDLINE

Search no.	Search terms	No. articles
1	Gingival recessions (free term)	334
2	Gingival recessions (MeSH)	272
3	#1 OR #2	273
4	Root coverage	116
5	#3 AND #4	107
6	Root surface conditioning	14
7	Root surface biomodification	4
8	#6 OR #7	16
9	#5 AND #8	8

Results

Literature Search and Study Characteristics

The MEDLINE search yielded 8 titles and abstracts; the Cochrane search did not produce any different studies. From these, 5 articles were deemed to meet the inclusion criteria and were read in full; 4 were considered relevant after data extraction and interpretation.

The manual searches resulted in 8 additional abstracts: 5 were selected, read in full and their data extracted; of these 2 were considered relevant.

Thus, 6 studies met the inclusion–exclusion criteria after a full reading (Table 2). The other 4 studies^{9,12,20,29} were excluded because they provided no information about recession characteristics, did not refer to Miller³⁰ classifications and lacked sample data.

Of the 6 included studies, semilunar coronally repositioned flap was used in 1,²¹ subepithelial connective tissue graft associated with coronally advanced flap (SE + CAF) was performed in 4,^{5,8,23,24} and free gingival graft was used in 1.¹¹ Regarding RSB in the test group, citric acid was used in 2 studies^{8,11}; EDTA 24% with different application methods in 2;^{21,22} and lasers with 2 different protocols in 2.^{23,24} All 6 studies included a 6-month follow-up.

Table 2 Randomized controlled trials included in this review, their root surface protocols and main outcomes

Author and year	Study group	Split-mouth	Surgery technique	Root surface protocol	Main outcome	Quality rating*
Bertrand et al. 1988 ¹¹	8 males 20 recessions	Yes	Free gingival graft	Citric acid, pH 1.0, 5 minutes	RSB with citric acid did not contribute any benefit in terms of outcome.	Fair
Caffesse et al. 2000 ⁸	14 males 22 females 36 recessions (control group 19; test group 17)	No	SE + CAF	Citric acid, pH 1.0, 1 minute	Citric acid demineralization did not affect clinical outcome of the treatment.	Fair
Kassab et al. 2006 ²²	5 males 5 females 20 recessions	Yes	SE + CAF	EDTA 24% in sterile distilled water, 2 minutes	The use of EDTA as a root conditioner did not provide any significant benefit.	Fair
Bittencourt et al. 2007 ²¹	9 males 6 females 30 recessions	Yes	Semi-lunar flap	EDTA 24% gel, pH 8.5, 2 minutes	The use of EDTA gel negatively affected root coverage outcome.	Good
Dilzis et al. 2010 ²³	8 males 9 females 34 recessions	Yes	SE + CAF	Nd:YAG laser, 2 irradiations	The use of Nd:YAG laser negatively affected root coverage outcome.	Fair
Dilzis et al. 2010 ²⁴	6 males 6 females 24 recessions	Yes	SE + CAF	Er:YAG laser, 2 irradiations	The use of Er:YAG laser did not enhance root coverage outcome.	Fair

*Good = meets all criteria; fair = does not meet all criteria but has no fatal flaw that would invalidate its results.

Note: EDTA = ethylenediaminetetraacetic acid; Er:YAG = erbium-doped yttrium aluminium garnet; Nd:YAG = neodymium yttrium aluminium garnet; SE + CAF = subepithelial connective tissue graft associated with coronally advanced flap.

None of the included studies reported any additional benefit from RSB. Furthermore, in 2 situations,^{21,23} the intervention in the test group had a negative impact on the treatment outcome.

Baseline–Outcome Comparisons

*Citric acid and free gingival graft*¹¹: The range of coverage for the control and test groups was 39–94% and 53–94%, respectively. Mean coverage was 66% and 74%, respectively. No significant difference was found between pre- and post-operative measures of recession, probing depth, amount of keratinized tissue and percentage root coverage.

*Citric acid and SE + CAF*⁸: Treatment produced a reduction in recession height (2.79 ± 0.79 mm for the control group and 2.56 ± 0.73 mm for the test group) and width (3.74 ± 1.19 for control group and 3.50 ± 0.73 mm for test group), an increase in keratinized tissue (2.47 ± 1.6 mm for control group and 2.3 ± 1.2 mm for test group) and no significant change in probing depth (-0.16 ± 0.06 mm for control group and -0.13 ± 0.81 mm for test group).

Thus, there were no statistically significant differences between groups.

*EDTA and SE + CAF*²²: There were no statistically significant differences between the control and test groups for pocket depth, increase in level of clinical attachment (4.1 mm for control group and 4.0 mm for test group) or root coverage (97.5% and 97.1%, respectively).

*EDTA and semilunar coronally positioned flap*²¹: Control and test groups showed 90.1% and 70.2% average root coverage and 66.7% and 40.0% complete root coverage, respectively. The control group showed a significant increase in width of the keratinized mucosa and a greater reduction in recession width and height. Root sensitivity was experienced by 9 patients before surgery and remained in 3 test group patients after conclusion of treatment. Thus, the use of EDTA negatively affected root coverage.

*Nd:YAG laser and SE+CAF*²³: Both groups showed improvement in recession dimensions and clinical

attachment levels. However, the control group showed greater reduction in recession depth and width. Similarly, average root coverage was 77% in the control group and 33% in the test group, and complete coverage was 65% and 18%, respectively. Thus, laser therapy negatively affected the results of the treatment.

*Er:YAG laser and SE+CAF*²⁴: There were no significant differences between groups. Root coverage and gain in clinical attachment levels were achieved. Average root coverage was 86% and 80% and complete coverage was 67% and 75%, for the control and test groups, respectively. Thus, RSB using the Er:YAG laser does not enhance the results achieved with SE + CAF alone.

Discussion

The importance of systematic reviews is well established, as they provide data for rational decision-making. The use of explicit methods allows assessment of what was done, limits bias and increases the reliability and accuracy of conclusions.^{27,31,32}

This review assessed the results of available randomized controlled trials where RSB was used before root coverage; strict inclusion criteria were imposed to enable an unbiased analysis and a conclusion regarding the impact of this practice on treatment results.

Only studies dealing with patients with Miller class I and II recession were chosen, as this is the gingival recession classification³⁰ most accepted and widespread; these are also the classes that show the highest success rates for root coverage. Some articles^{9,11,12,20} that did not refer to Miller classes, as this scheme had just been published at the time of the studies, might have been included; however, the lack of any description of recession characteristics, such as mean depth and the presence of interdental bone, resulted in their exclusion.

Some articles^{13,33} seemed relevant, but during evaluation of data, it was observed that different surgical approaches had been used for the control and test groups. Therefore, despite the use of RSB in test group, these articles were excluded as the additional variable affecting treatment outcome was beyond the scope of this review.

Similarly, studies including smokers were excluded because evidence of the negative impact

Table 3 Publications excluded after full-text evaluation and main reasons for exclusion

Author (year)	Intervention	Reason for exclusion
Oles et al. (1985) ²⁰	Citric Acid	No information about recession characteristics or reference to Miller ³² classifications and lack of sample data.
Ibott et al. (1985) ¹²	Citric Acid	No information about recession characteristics or reference to Miller ³² classifications and lack of sample data.
Caffesse et al. (1987) ²⁹	Citric Acid	No information about recession characteristics or reference to Miller ³² classifications and lack of sample data.
Oles et al. (1988) ⁹	Sodium Hypochlorite	No information about recession characteristics or reference to Miller ³² classifications and lack of sample data.

of smoking on the success rates of periodontal therapy, including root coverage, has been well reported in the literature.³⁴ These studies were also excluded for not presenting a description of recession characteristics.

Despite the widespread use of tetracycline for RSB,¹³ no studies dealing with this agent matched the selection criteria for our review.

Root sensitivity is usually the main complaint of patients who present with gingival recession.⁵ This sensitivity seems to increase when EDTA or citric acid is used in RSB. Surprisingly, only 1 of the analyzed studies²¹ reported data concerning root sensitivity before and after root coverage. After treatment, only patients submitted to RSB complained about root sensitivity, which could possibly be related to the demineralization promoted. The lack of this information from other studies limits comparisons among RSB protocols.

The absence of further post-operative complications may be related to the follow-up period. One study³⁵ reported cervical root resorption 20 months after RSB with tetracycline, and the authors suggest that this long-term complication occurred as a result of the use of tetracycline. Similar conclusions were also found in another study.³⁶ It is important to note that all studies

included in this review included 6-month follow-up. We presume that long-term evaluations are necessary to provide sufficient data to reach proper conclusions concerning this issue.

Even though laser therapy has been widely studied in periodontics for pocket debridement, wound healing and in surgical approaches,³⁷ no benefits were found from its bioestimulation³⁸ in either of the 2 RSB protocols.^{23,24}

The variety of RSB protocols (EDTA gel, EDTA in sterile water, citric acid at various concentrations and laser application) associated with surgical procedures, such as SE + CAF and semilunar coronally positioned flap, makes inter-study comparison impossible. The lack of consensus on the best protocol is pervasive.

Currently, several biomaterials, such as bone morphogenetic protein (BMP) and platelet-derived growth factor (PDGF), have shown promising results when applied to the root surface. In dogs, root surfaces conditioned with BMP stimulated cementum-like tissue formation and inhibited epithelial downgrowth.³⁹ Good results were also achieved with PDGF, as it provided good root surface biocompatibility and had a positive effect on adhesion and growth of cultured fibroblasts on periodontally diseased surfaces.^{40,41} However, randomized controlled trials are required to confirm the benefits of these materials in terms of root coverage.

Preliminary results show that enamel matrix proteins, in combination with CAF — regardless of whether they are associated with connective tissue graft for the treatment of Miller class I or II gingival recession — produce good clinical results, with root coverage comparable or superior to other techniques. Further experimental studies on the dynamics of wound healing are needed to prove that enamel matrix proteins are really responsible for improving the percentage of regenerated versus repaired tissues in other techniques.⁴²

Notwithstanding the probable benefits of biomaterials in promoting or inducing tissue regeneration, they are not usually considered RSB agents²⁴ because they do not aim to remove a smear layer and expose the collagen matrix.¹⁹

Although other articles have discussed RSB, none has addressed it as the main variable. In fact, the variety of RSB agents used in clinical practice

in combination with multiple mucogingival techniques makes the establishment of an accurate protocol difficult. In addition, recent studies^{23,24} have reported modalities, such as laser therapy, not studied for this purpose so far. As this subject is still being studied, subjected to clinical trials and used in periodontal practice, sometimes based on unverified beliefs, the doubt concerning the efficacy of RSB agents remains a subject of discussion.

Finally, based on this systematic review, it is evident that the use of RSB agents does not improve root coverage outcomes. Depending on the protocol adopted, RSB can even worsen the results of treatment. Thus, the use of any modality of RSB associated with root coverage should be reconsidered as no evidence of its efficacy is available in the literature unless new randomized controlled trials with well-designed methods present different conclusions.

Conclusion

Within the limitations of this systematic review, it is possible to conclude that all mucogingival surgery approaches used in the selected studies achieved a high rate of success in terms of root coverage; none of the RSB protocols reviewed produced any advantage to justify their use in root coverage procedures; and there is no evidence to support RSB prior to root coverage. ♦

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