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## Abstract

Previous systematic review reported similar results of periodontal therapy when full mouth disinfection (FMD) and multi-session periodontal therapy (MST) were compared for treatment of chronic periodontitis (CP). However, this comparison has not been performed for treatment of Aggressive periodontitis (AP). The aim of this systematic review was to compare the results of FMD and MST in individuals with AP. Electronic searches for Randomized Clinical Trials (RCT) were performed in five electronic databases up to April 2016. A manual search was also performed in 4 periodontal journals for papers published in the last 15 years. The primary outcomes were changes in probing depth, clinical attachment loss and bleeding on probing. The secondary outcomes were changes in the plaque and marginal gingival bleeding scores, degree of furcation defect, gingival recession, microbiological changes and side effects. The results found 4RCTs that were included in the review, only 2 of which described treatment in different populations. The differences between periodontal approaches are minimal and the use of systemic antibiotics appears to add additional improvement, although with uncertain clinical relevance. The analysis of methodological quality demonstrated a high risk of bias, which weakens the internal validity of the evaluated studies. Moreover, FMD has a higher frequency of side effects, such as fever and labial herpes. Further randomized clinical trials are needed to establish the clinical relevance of FMD for the treatment of aggressive periodontitis.

Keywords: Antibiotics; Chlorhexidine; Aggressive periodontitis; Periodontal debridement

## Introduction

Aggressive periodontitis (AP) is a multifactor immuno inflammatory condition with rapid, severe progression that mainly affects young individuals. AP seems to occur by the interaction of specific pathogens and host susceptibility [1]. Individuals diagnosed with AP exhibit considerable bacterial diversity, but the species that are more strongly associated with AP are *Porphyromonas gingivalis, Tannerella forsythia* and *Aggregatibacter actinomycetemcomitans*, along with a high prevalence rate and proportion of the genus *Selenomonas* in affected sites [2]. Environmental and genetic influences also play an important role in the susceptibility of individuals affected by AP, as the variability of the clinical results may be related to individual inflammatory responses [3,4].

Considering that it is still improbable to alter genetic susceptibility, mechanical periodontal therapy is restricted to suppress the target periodontal species and expedite the establishment of a host compatible microbiota over time [5]. However, mechanical therapy alone is sometimes insufficient to control the progression of periodontitis in individuals with AP [6,7]. Thus, alternative complementary therapies have been proposed to achieve more beneficial and stable bacterial recolonization in recently scaled pockets, such as the administration of systemic antibiotics that acts by suppress in pathogenic bacterial species during periodontal therapy [8-10].

Periodontal therapy with scaling and root planning (SRP) by quadrants or sextants in short sessions over few weeks has been widely performed [11]. However, some studies suggest that this strategy may favor the re-infection of treated periodontal pockets through other niches, such as untreated periodontal pockets, tongue, tonsils, mucosa and saliva [12-14]. In order to minimize the re-colonization of

recently treated sites, full mouth disinfection (FMD) approach has been employed in periodontal therapy. FMD consists of SRP of all periodontal pockets within 24 hours [13,15]. A systematic review on the treatment of chronic periodontitis (CP) reports similar results with FMD and multi-session periodontal therapy (MST) [16,17].

823

Evidence-based knowledge supports that periodontal tissue damage is probably the result of an excessive host response, in which excess cytokines, reactive oxygen species and metallo proteinases are generated and overwhelm their respective antagonists (e.g., antioxidants and tissue inhibitors of matrix metallo proteinases) [18]. This incipient dysbiosis in host response may be higher in individuals with AP comparing to CP [19]. This hypothesis is reinforced by response to periodontal therapy, while some studies reported similar short-term results between CP and AP [20,21] where as others report worse periodontal response following MST in individuals with AP [22-24]. Considering this higher host response with reduced levels of interleukin-10 and IgG and increased periodontal pathogens [19, 22,24] bacterial translocation following MST may result in worse response of periodontal therapy in subjects with AP. However, according to our knowledge there is no previous systematic review that has compared FMD to MST in individuals with AP; Thus, the aim of the present study was to systematically analyze randomized clinical trials (RCTs) to determine the best approach (FMD versus MST) for the treatment of AP.

## **Materials and Methods**

#### Study protocol

The study protocol was structured based on the recommendations of the Cochrane Collaboration [25] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [26]. The protocol is registered with the International Prospective Register of Systematic.

## **Focused** question

The following question guided the present investigation: "What is the effectiveness of FMD with or without adjunct antibiotic therapy in comparison to MST for the treatment of AP?"

#### Search strategy

We conducted an electronic search of the Pubmed/MEDLINE, Cochrane-CENTRAL, EMBASE, TRIP, ISI Web of Science and LILACS databases to identify relevant literature published through 15April 2016. The Pubmed/MEDLINE search was performed using a combination of controlled vocabulary and key words, as follows:

**Patients:** ("aggressive periodontitis" [MeSH Terms] OR "juvenile periodontitis" [All Fields]) OR "early onset periodontitis" [All Fields]) OR "aggressive periodontitis" [All Fields]).

Intervention: ("periodontal therapy" [All Fields] OR "periodontal non surgical treatment" [All Fields]) OR "periodontal treatment approach" [All Fields]) OR "periodontal treatment methods" [All Fields]) OR "periodontal treatment modalities" [All Fields]) OR "periodontal treatment modality" [All Fields]) OR "scaling root planing" [All Fields]) OR "dental scaling" [All Fields]) OR "calculus removal" [All Fields]) OR "calculus debridement" [All Fields]) OR "periodontal debridement" [All Fields]) OR "cot planing" [All Fields]) OR "non surgical treatment" [All Fields]) OR ("Periodontal Debridement" [Mesh] OR "Subgingival Curet-tage" [Mesh] OR "Dental Scaling" [Mesh] OR "Dental Scaling" [Mesh]) OR "Dental Scaling" [Mesh]) OR "Dental Scaling" [Mesh]) OR "Metronidazole" [Mesh]) OR disinfection" [All Fields]) OR "full mouth disinfection approach" [All Fields]) OR "full mouth debridement" [All Fields]) OR "full mouth periodontal "[All Fields]) OR "full mouth non surgical periodontal" [All Fields]) OR "full mouth debridement" [All Fields]) OR "full mouth periodontal "[All Fields]) OR "full mouth non surgical periodontal" [All Fields]) OR "full mouth root planing" [All Fields]) OR "full Fields]) OR "full mouth periodontal surgery" [All Fields]) OR "full mouth root planing" [All Fields]) OR "full Fields]) OR "full mouth root planing" [All Fields]) OR "full Fields]) OR "amoxicillin metronidazole combination therapy" [All Fields]) OR "amoxicillin metronidazole combination therapy" [All Fields]) OR "amoxicillin metronidazole group" [All Fields]) OR "amoxicillin metronidazole combination therapy" [All Fields]) OR "amoxicillin metronidazole group" [All Fields]) OR "amoxicillin metronidazole combination therapy" [All Fields]) OR "amoxicillin metronidazole group" [All Fields]) OR "amoxicillin metronidazole combination therapy" [All Fields]) OR "amoxicillin metronidazole group" [All Fields]) OR "amoxicill

824

Likewise, a similar search strategy was adapted for the other databases. We also searched for relevant on going trials in the Clinical Trials Registry (http://www.clinicaltrials.gov), and we searched the grey literature (Open Grey). We manually searched the reference lists of all full texts of interest and the tables of contents of the Journal of Clinical Periodontology, Journal of Periodontal Research, Journal of Periodontology and Periodontology 2000. References of potentially eligible papers and review articles were also checked. To minimize selection bias, no restrictions were made regarding language and all references in the articles selected were analyzed.

## Selection of papers and data collection

In the first phase of the selection process, studies were included or excluded based on the title. In the second phase, eligibility was based on the reading of the abstract. In the third phase, full texts were analyzed. Two blinded researchers (R.P.A. and F.B.Z.) evaluated the articles in each phase, independently. At the end of each phase, divergences were discussed until a consensus was reached. The papers were selected based on the eligibility criteria. The reviewers showed kappa scores of 0.92 (titles and abstracts) and 0.88 (full texts).

## **Eligibility criteria**

The following eligibility criteria was considered: Randomized and/or controlled clinical trials; studies involving good general health humans (no systemic disorders), of both genders, aged 18 years or older, with a diagnosis of AP [1]; comparison of MST to FMD (defined as SRP in all quadrants within 24 hours) with or without chlorhexidine and/or antibiotic therapy in both groups; and at least six months of follow up. Studies that used only FMD or MST, those that evaluated patients with any systemic disease or made use of medication with a known effect on periodontal tissues and/or treatment in the three months prior to the study, duplicate studies and those that did not analyze the primary outcomes of interest were excluded from the review.

#### **Outcome variables**

Primary outcomes: changes in probing depth (mm), bleeding on probing (SS) and clinical attachment loss (mm).

**Secondary outcomes:** changes in plaque index, gingival bleeding index, degree of furcation defect, gingival recession, microbiological analyses, side effects and complications with the use of antibiotics.

#### Quality assessment

The methodological quality and risk of bias were evaluated by two independent researchers (R.P.A. and F.B.Z.) using the criteria proposed by the Cochane Collaboration described in the Cochrane Handbook for Systematic Reviews of Interventions [25]: sequence generation, allocation concealment, blinding, incomplete outcome data, selected outcome different from the protocol, adequate outcome reporting and potential threats to validity, such as improper calibration, improper sample size calculation, study design bias, etc. Using these criteria, the papers were classified with having a low, high or uncertain risk of bias. If a study exhibited a high risk of bias in at least one domain, it was considered to have a high risk of bias.

#### Assessment of heterogeneity

Two researchers collected the data independently (R.P.A and F.B.Z.). The following factors were recorded to investigate the interstudies heterogeneity of the primary outcomes: study design, number, age and age range of subjects, diagnostic criteria, number of teeth before and after treatment, smoking and intervention and control groups. When data were presented numerically in tables or text and graphically in figures, only the numeric data were considered. Divergences between the researchers were resolved by discussion until reaching a consensus.

## Data analysis and presentation

The data presentation is largely descriptive. Meta-analysis was precluded due to the small number of papers and considerable variation in the methodologies employed.

## Results

## Search results

Figure 1 shows the study selection process. The electronic and manual searches led to the identification of 1.611 potentially relevant papers, 254 were duplicates, 1328 of which were excluded based on the title. Thus, 29 papers were selected for the analysis of the abstract, and 23 did not meet the eligibility criteria, leaving six papers for full-text analysis. One of these papers was excluded for comparing FMD and SRP per quadrant in patients with CP followed up for only three months. The other paper was excluded because it did not define the type of periodontal disease and the period of follow-up was only three months (Table 1). Thus, four papers were included in the present systematic review.



Figure 1: Flowchart of selection process.

*Citation:* Maísa Casarin., *et al.* "Full Mouth Disinfection Versus Scaling and Root Planing per Quadrant in Aggressive Periodontitis: A Systematic Review". *EC Dental Science* 4.4 (2016): 822-834.

Authors, Years	Reason of Rejection
Graziani., et al. [31]	Not define type of periodontal disease and followed up for only three months.
Zijnge., <i>et al.</i> [32]	Chronic Periodontitis. Test group (FMD) and control group (per quadrant) and followed up for only three months.

Table 1: Summary of the Excluded Articles for full-text analysis.

#### **Characteristics of selected papers**

All four papers included in the present review were parallel-group randomized clinical trials, three of which described the results of the same patients that outcomes was explored in three different publications. Therefore, the information from these three papers was grouped and considered as a single article. Three papers were conducted in Belgium [27-29] and one was conducted in Brazil [30]. Sample size ranged from 12 to 34 participants and maximum follow up was eight months. One study only described the microbiological outcome [28] and another one described just clinical outcomes [30]. The sample from the Belgian study included smokers. The FMD protocol differed between the Belgian and Brazilian groups. In the Belgian group, FMD was completed in 24 hours, with three subgingival irrigations per session with 10-minutes interval using 1% chlorhexidine gel, the participants brushed the dorsum of the tongue for 60 seconds with 1% chlorhexidine gel, used a mouthwash with 0.2% chlorhexidine twice a day and performed tonsil disinfection with 0.2% chlorhexidine spray twice a day for two consecutive months [27-29]. In the Brazilian group, FMD was completed in 24 hours by two sessions of two-hours each, amoxicillin (500mg) and metronidazole (250 mg) were taken three times a day for seven days beginning immediately after the first SRP session and a 0.12% chlorhexidine mouthwash was used twice a day for two months [30]. Tables 2 and 3 show the characteristics of the four papers included in the review.

Author (year) and Number	Population	Criteria for definition of aggressive Periodontitis	Methodologi- cal Charac- teristics	Supragingival Control	Test Intervention	Control In- tervention	Follow-up Period	Side Effects
Quirynen., et al. [28] Mongar- dini., et al. [29] De Soete., et al. [27]	16 patients, Dep. of Periodontol- ogy, Hospital of University of Leuven, Belgium Test group: 3 F/5 M; Age: 34.3 +/- 5.8 *4 smokers Control group: 6 F/ 2 M; Age: 34.6 +/- 7.6; * 2 smokers	- Age versus n° of teeth involved; - frequency of angu- lar bone defects; - severity of de- struction in relation to age; - $\geq$ 6 sites with probing depth $\geq$ 7 mm + bleeding on probing + radio- graphic bone loss $\geq$ 50% in 1 <sup>st</sup> quadrant; - 26% ± 7.8% with probing depth $\geq$ 7 mm in 1 <sup>st</sup> quadrant	-Parallel- group randomized clinical trial	After 1 <sup>st</sup> session of scaling with re-instruction after 1, 2 and 4 months; Additional supragingival polishing at 2-month visit; *Dentifrice Sensodyne™ F-gel made available to all participants	FMD completed in 24 hours, brushing of dorsum of tongue for 60 seconds with 1% chlorhexi- dine gel; three subgingival irri- gations with 1% chlorhexidine gel at 10-min intervals; 0.2% chlorhexidine mouthwash twice a day for 2 months; disinfection of tonsils with 0.2% chlorhexi- dine spray twice a day *No antibiotic	Conventional multi-session (MST) per quadrant in one-hour sessions with two-week intervals; * No antibi- otic	8 months	Test group: Fever ≥ 37.5 °C: 10 patients rang- ing from 37.5 to 39.5 °C after final- ization of FMD; Labial herpes: 3 patients Oral ulceration: 1 patient Control group: Fever 37.5 to 38.0 °C: 3 patients Labial herpes: 1 patient Oral ulceration: 4 patient

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827	

Moreiraand	30 patients,	*Age 18 to 35 years;	-Parallel-	-	FMD completed	Conventional	6 months	Test group
Feres-Filho	non-		-group rando-		in 24 hours, 2	multi-session		
[30]	smokers,	*At least 20 teeth	mized clinical		two-hour ses-	(MST) per		Pain: 54%
[30]	smokers, Postgraduate program in Periodontol- ogy, School of Dentistry, Federal Uni- versity of Rio de Janeiro, Brazil <b>Test group:</b> 86,7% F/13,3% M; Age: 28.4 +/- 5.7 <b>Control</b> <b>group:</b> 87% F 13% M; Age: 29.5	*At least 20 teeth present; *≥ 4 sites in dif- ferent teeth with probing depth ≥ 6 mm and clinical attachment loss ≥ 5 mm; *Bone loss ≥ 50% in majority of teeth with periodontitis	mized clinical trial		two-hour ses- sions; Amoxicillin (500 mg) and metro- nidazole (250 mg) 3x a day for 7 days begun im- mediately after 1 <sup>st</sup> SRP session; 0.12% chlorehxi- dine mouthwash twice a day for 2 months	(MST) per quadrant in one-hour sessions with two-week intervals; Amoxicillin (500 mg) and metronidazo- le (250 mg) 3x a day for 7 days begun immediately after 1 <sup>st</sup> SRP session; 0.12% chlorehxidine mouthwash twice a day for 2 months		Pain: 54% Fever (> 37 °C): 47% <sup>∞</sup> Labial herpes: 47% <sup>∞</sup> <b>Control group:</b> Pain: 47% Fever (> 37°C): 6% <sup>∞</sup> Labial herpes: 0% <sup>∞</sup>

Table 2: Characteristics of studies included in review.

M: masculine; F: Female; FMD: Full mouth disinfection; MST: Multi-session periodontal therapy.

## **Risk of bias**

The risk of bias was only analyzed in the studies that described clinical outcomes [29, 30]. In the pooled Belgian papers, this analysis was performed on the investigation that evaluated the primary outcomes [29]. Both studies received an uncertain score regarding the participant's allocation concealment because there was no further information about this process description [29,30]. One study received a negative score for blinding, as the treatments and clinical exams were performed by the same researcher throughout the entire study [30]. The other study only presented data on the 1<sup>st</sup> quadrant and therefore received negative scores for complete outcome data and adequate outcome reporting [29]. Both studies were classified as uncertain score regarding to other threats to validity due to incomplete information on the calibration exercise and no description of the sample size calculation. Table 4 displays the risk of bias in the studies.

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Author (Year)	Supragingival Control	Probing Depth	Clinical Attachment Loss	Bleeding On Probing	Other Outcomes
Quirynen <i>et al.</i> 1999 [28]	Test group:	Test group (n=8):	Only data on $1^{st}$ quadrant	*Only data on 1 <sup>st</sup> quadrant	Microbiological out- comes
Mongardini <i>et a</i> l. 1999 [29]	Gingival bleeding index: Baseline: 0.7 ± 0.5 8 months: 0.05	*Only data on 1 <sup>st</sup> quadrant *Data from study by Mongardini et al. (1999) [29] Sites with initial probing depth ≥ 7 mm:	*Data from study by Mon- gardini et al. (1999) [29] *Only gain in clinical at- tachment represented graphically (without data on initial and final values)	*Data from study by Mon- gardini et al. (1999) Test group:	*Only data on 1 <sup>st</sup> quadrant *Collection from sites with initial probing depth ≥ 7 mm for single-root
De Soete <i>et al.</i> 2001[27]	± 0.1 Quigley & Hein plaque index	Single-root teeth (Base: 7.9 mm - 8 months: 5.0 mm) = $\Delta$ : 2.9 mm; Multi-root teeth: (Base :8.1 mm - 8 months: 6.0 mm) = $\Delta$ : 2.1 mm	Test group Sites with initial probing depth $\geq$ 7 mm:	Baseline: 74%±30 8 months:	and multi-root teeth; Ini- tial probing depth ≥ 4.5- 6.5 mm for single-root and multi-root teeth;
	Baseline: 2.21±0.5	Sites with initial probing depth $\ge$ 4.5-6.5 mm:	Single-root teeth: 1.3 mm	31%±11∞ Δ=43%	Data from study by Qui- rynen et al. (1999) [28]
	8 months: 0.85±0.4∞ Control group:	Single-root teeth (Base: 5.5 mm – 8 months: $3.9 \text{ mm}$ ) = $\Delta$ : 1.6 mm;	Multi-root teeth: 0.9 mm Sites with initial probing depth $\ge 4.5-6.5$ mm:	Control group: B a s e l i n e :	*Collection from 4 deep- est proximal sites in each subgroup;
	Gingival bleeding	Multi-root teeth: (Base: 5.5 mm – 8 months: 3.8 mm) = $\Delta$ : 1.7 mm	Single-root teeth: 1.2 mm $^{\circ}$	86%±14 8 m o n t h s :	*Collection from mucos dorsum of tongue an saliva;
	Baseline: 0.87 ± 0.5	Control group (n=8): Sites with initial probing depth ≥ 7 mm:	Multi-root teeth: 1.0 mm <sup>∞</sup> Control group:	47%±10∞ Δ=39%	*Dark field microscopy and cultures in anaero biosis (CFUs/ml)
	8 months: 0.14 ± 0.1	Single-root teeth: Base: 7.8 mm – 8 months: 5.7 mm) = $\Delta$ : 2.1	Sites with initial probing depth $\geq$ 7 mm:	*16% differ- ence favoring test group	No significant difference between test and con-
	Quigley & Hein plaque index Baseline: 2.03±0.7 8 months: 1.06±0.5∞	mm; Multi-root teeth:	Single-root teeth: 0.8 mm Multi-root teeth: 1.05 mm	test group	trol group for all vari- ables and subgroups at 8 months
		Base: 8.1 mm – 8 months: 6.3 mm) = Δ: 1.8 mm;	Sites with initial probing depth $\geq$ 4.5-6.5 mm:		Data from study by De Soete et al. (2001) [27]
		Sites with initial probing depth $\ge$ 4.5-6.5 mm:	Single-root teeth: 0.3 mm∞		*Collection from 4 deep est proximal sites in each
		Single-root teeth (Base: 5.5 mm – 8 months: 4.1 mm) = $\Delta$ : 1.4 mm;	Multi-root teeth: 0.4 mm <sup>∞</sup> *Difference between FMD and MST		subgroup; *Checkerboard DNA-DNA hybridization
		Multi-root teeth (Base: 5.4 mm – 8 months: $3.9 \text{ mm}$ ) = $\Delta$ : 1.5 mm	Initial probing depth ≥ 4.5- 6.5 mm:		* Only descriptive data of mean proportions, with
		*Difference between FMD and MST Initial probing depth ≥ 4.5-6.5 mm:	Single-root teeth: 0.9 mm; Multi-root teeth: 0.6 mm		no statistical analysis; *Slight differences favor
		Single-root teeth: 0.2 mm; Multi-root teeth: 0.2 mm favoring test group	favoring test group Initial probing depth $\geq$ 7		ing test group for red and orange complexes, espe cially in single-root teeth
		Initial probing depth $\geq$ 7 mm:	mm: Single-root teeth: 0.5 mm; Multi noot tooth: 0.25 mm;		*Lower frequencies o P. gingivalis, T. forsythia
		Single-root teeth: 0.8 mm; Multi-root teeth: 0.3 mm favoring test group	Multi-root teeth: 0.25 mm favoring test group		and A. agregatibacter in test group

Author (Year)	Supragingival	Probing Depth	Clinical Attachment Loss	Bleeding On	Other Out-
Author (rear)	Control	Trobing Depth	chincal Attachincht 2055	Probing	comes
	Test group	Test group	Test group	Test group:	Only clinical out-
					comes analyzed
	Visible plaque	Sites with initial probing	Sites with initial clinical at-	Baseline:	
	Baseline: 48.5%±3.6%	depth ≥ 7 mm:	tachment loss ≥ 7 mm:	45.7%±4.7	
		Base: 7.7 mm ± 0.6 – 6	Base: 8.1 mm ± 0.9 – 6	6months:	
Moreira and	6months: 6.3%±1.0%∞	months: $3.2\pm0.3$ mm = $\Delta$ :	months: $3.9 \pm 1.0 \text{ mm} = \Delta$ :	6.0%±0.9∞	
Feres-Filho, 2007		4.5 mm;	4.2 mm;		
[30]				Δ=39%	
	Control moun	Sites with initial probing	Sites with initial clinical at-		
	Control group	depth 4-6 mm:	tachment loss 4-6 mm:		
	Visible plaque	Base: 4.7 mm ± 0.2 – 6	Base: 5.3 mm ± 0.8 – 6	Control group:	
		months: $3.6 \pm 0.1 \text{ mm} = \Delta$ :	months: $3.6\pm0.7$ mm = $\Delta$ :		
	Baseline: 49%±4,5%	1.1 mm;	1.7 mm;	Baseline:	
	6 months: 9.8%±2.3∞			51.9%±3.1	
				6months:	
		Control group	Control group	8.9%±1.9∞	
	*No data on marginal	Sites with initial probing	Sites with initial clinical at-		
	bleeding	depth $\ge$ 7 mm:	tachment loss ≥ 7 mm:	Δ=43%	
		Base: 7.8 mm ± 0.8 – 6	Base: 7.9 mm ± 0.8 – 6		
		months: $3.1\pm0.5$ mm = $\Delta$ :	months: $4.1\pm1.2 \text{ mm} = \Delta$ :	* 4% difference	
		4.7 mm;	3.8 mm;	favoring control	
				group	
		Sites with initial probing	Sites with initial clinical at-	group	
		depth 4-6 mm:	tachment loss 4-6 mm:		
		Base: 4.8 mm ± 0.2 – 6	Base: 5.0 mm ± 0.3 – 6		
		months: $3.4\pm0.2$ mm = $\Delta$ :	months: $3.4\pm0.5 \text{ mm} = \Delta$ :		
		1,4 mm;	1.6 mm;		
		*Difference between FMD	*Difference between FMD		
		and MST	and MST		
		Initial probing depth 4-6	Initial clinical attachment		
		mm: 0.3 mm favoring con-	loss 4-6 mm: 0.1 mm favor-		
		trol group;	ing test group;		
		Initial probing depth ≥ 7	Initial clinical attachment		
		mm: 0.2 mm favoring con-	loss ≥ 7 mm: 0.4 mm favor-		
		trol group.	ing control group.		

Table 3: Outcomes in studies included in review.

	Adequate generation of randomization sequence	Allocation con- cealment	Blinding	Complete out- come data	Adequate out- come reporting	Other threats to validity
Quirynen <i>et a</i> l. 1999 [28] Mongardini <i>et al.</i> 1999 [29] De Soete <i>et al.</i> 2001[27]	+	?	+	-	-	?
Moreira and Feres- Filho, 2007 [30]	+	?	-	+	+	?

? = not specific/unclear; + = yes; - = no

#### Table 4: Quality of studies selected.

## Summary of clinical findings

In the analysis of the reduction in probing depth, Mongardini *et al.* [29] found no statistically significant differences between the FMD and control groups (MST) for teeth with moderate pockets, as the test group had better results (0.2 mm differences) for both single-root and multi-root teeth [29]. Moreover, no significant differences were found for teeth with deep pockets, as the test group had better results with 0.8 mm for single-root teeth and 0.3 mm for multi-root teeth. Moreira and Feres-Filho [30] who did not perform separate analyses for single-root and multi-root teeth, found a 0.3 mm difference favoring the control group in moderate pockets and an 0.2 mm difference favoring the control group in deep pockets [30].

In the evaluation of clinical attachment loss, Mongardini *et al.* [29] found statistically significant differences (P<0.05) of 0.9 mm and 0.6 mm in moderate pockets of single-root and multi-root teeth, respectively, favoring the FMD group compared to MST group [29]. In the deep pockets, the differences were 0.5 mm and 0.25 mm for single-root and multi-root teeth, respectively, also favoring the FMD group. Moreira and Feres-filhos [24] found a difference of 0.1 mm for teeth with moderate pockets favoring the FMD group and a difference of 0.4 mm for teeth with deep pockets favoring the control group, but these differences did not achieve statistical significance [30].

Mongardini *et al.* [29] found a statistically significant difference (16%) regarding the bleeding on probing favoring the test group [29]. In contrast, Moreira Feres-Filho found a non-significant difference (4%) favoring the control group [30]. Significant differences regarding the visible plaque index favoring the test group were found in both studies [29,30]. The gingival bleeding index was only analyzed in one of the studies, which report no clinical relevant differences in the eighth month (test group:  $0.05 \pm 0.1$ ; control group:  $0.14 \pm 0.1$ ) [29].

## Summary of microbiological findings

Two studies analyzed microbiological outcomes. Quirynen *et al.* [28] analyzed samples from the tongue, mucosa, saliva and the four deepest proximal sites of single-root and multi-root teeth using dark field microscopy and cultures in anerobiosis (colony-forming units/ ml), but did not find significant differences between the test and control groups [28]. De Soete *et al.* [27] analyzed four proximal sites of single-root and multi-root teeth using Checkerboard DNA-DNA hybridization and found a slightly greater reduction in microorganisms of the red and orange complexes, especially in single-root teeth, as well as lower frequencies of *P. gingivalis, T. forsythia* and *A. actinomy-cetemcomitans* in the test group [27].

## Discussion

The reduction in the occurrence of bacterial re-infection constitutes the main potential advantage of FMD versus MST for the treatment of AP, since periodontal pathogens that colonize different niches in the oral cavity can move into previously treated sites [13]. However, according to the reviewed studies this potential advantage of FMD treatment has resulted in minor clinical results improvement. This results are in accordance to previous systematic review comparing FMD and MST for treatment of chronic periodontitis [16].

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831

The methodological differences regarding the procedures and criteria employed hinder the direct comparison of the studies included in this review. The complementary use of antibiotic was employed in one study [30] and not in the other [29]. Moreover, the latter study included smokers. Determination of baseline probing depth and clinical attachment loss was performed prior to the initial SRP in one study [30] and after the initial SRP in the other [29]. Thus, the diagnostic precision can be altered, as the presence of subgingival calculus can lead to lower probing depth prior to the initial SRP [33] where as the trauma caused by prior SRP can lead to deeper probing depths following the procedure. Clinical and microbiological analyses were only performed in the 1<sup>st</sup> quadrant in one study [29] which did not provide information regarding the effect of both periodontal approaches [34]. The follow-up period was also differed (six months [30] and eight months [29]). All these characteristics explain the different clinical magnitudes in the findings of the two studies. Moreover, the high risk of bias compromises the internal validity of the analyzed studies.

Generally, the differences between FMD and MST strategies within the studies were non-significant for the most analyzed variables. Significant differences favoring the FMD group were found only in one study for clinical attachment loss (0.5 mm and 0.9 mm for singleroot teeth with moderate and deep pockets, respectively, as well as 0.6 mm and 0.25 mm for multi-root teeth with moderate and deep pockets, respectively). Moreover, a 16% difference in bleeding on probing favoring the FMD treatment in the same study. However, the high percentage of bleeding in both groups following treatment indicates a poor periodontal response for both strategies [35]. In the Brazilian study, periodontal treatment was more effective in both groups when considering the changes in bleeding on probing, probing depth and clinical attachment loss [30]. These differences may be explained by the non-inclusion of smokers in the Brazilian study. Previous studies demonstrated that smoking exerts a negative influence on clinical results in the treatment of generalized AP [36,37]. Another point to be highlighted is the use of antibiotics as complementary treatment in one of the studies [30]. A recent meta-analysis suggests an additional clinical benefits when amoxicillin and metronidazole are used to complement FMD in patients with AP [38]. Moreover, it must be considered the side effects of therapy, on cerelevant differences were found between FMD and MST in both studies, with the occurrence of fever and labial herpes in the FMD treatment.

In both studies, the periodontal treatment was carried out into a short period (1/h per quadrant independently of the type of approach). As the studies have included patients diagnosed with advanced periodontitis, time spent to the treatment may be considered too short for an adequate disinfection of the root surface. It has been demonstrated that longer subgingival procedures offer a better clinical results following periodontal non-surgical treatment of AP [39]. Thus, it's possible to hypothesize this therapeutic strategy would be more beneficial in the treatment of AP than CP, since the residual bacterial load in periodontal pockets appears to be more easily decreased combated in patients with CP [4] apparently due to the complementary use of antibiotics.

FMD for advanced generalized AP seems to offer additional benefits due to the positive correlation between the severity of periodontitis and the bacterial count in the saliva. Periodontal treatment has a positive effect on reducing the number of bacteria in the saliva as well as *de novo* plaque formation [40, 41] and it appears that disinfection of the periodontal pockets in a short period slows down *de novo* plaque formation [42]. On the other hand, patient adherence to supragingival plaque control is often difficult to predict. Thus, supragingival control prior to subgingival interventions appears to be rational and also exerts an influence on *de novo* plaque formation, as the extent of gingivitis is also correlated with the rate of *de novo* plaque formation [42].

#### Conclusion

A small number of RCTs, methodological limitations and heterogeneity between included studies do not allow drawing a clear conclusion to our focused question. Besides the limitations of this review, as the small number of RCTs included ant the heterogeneity of the studies, the FMD approach seems to present in slight better results on the treatment of moderate and advanced periodontal pockets when compared to MST. However, the clinical significance of these differences is questionable and may be irrelevant. Thus, the decision regarding the type of clinical approach to be used on the periodontal treatment should be based considering the costs, benefits and side effects of each therapy the professional skills and the patient profile. Furthermore, further RCTs comparing FMD and MST approaches are necessary to validate or refute these findings.

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