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ORIGINAL ARTICLE

Different scaling and root planing strategies in Turkish patients with aggressive periodontitis: A randomized controlled clinical trial

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Abstract

Objectives: The aim of this study was to compare clinical, cytokine and microbiological responses after quadrant-based scaling and root planing (Q-SRP), full-mouth SRP (FM-SRP) and full-mouth disinfection (FMD) in patients with generalized aggressive periodontitis (GAgP), which is currently termed as generalized stage-III and grade-C periodontitis.

Methods: Forty-two patients with GAgP were randomly assigned into groups as Q-SRP, FM-SRP or FMD with chlorhexidine. Clinical parameters were recorded, and gingival crevicular fluid (GCF) and subgingival plaque samples were collected at baseline, 3 and 6 months after treatment. GCF levels of interleukin (IL)-1β and IL-17 were analysed using ELISA. Quantities of six bacterial species were determined using qPCR.

Results: Clinical parameters improved significantly in all groups at 3 and 6 months ($p < 0.05$). Percentage of sites with probing depth >6 mm was lower in the FMD than Q-SRP group at 3 and 6 months ($p < 0.05$). FMD showed significantly higher percentage of pocket closure compared with Q-SRP and FM-SRP at both 3 and 6 months after treatment ($p < 0.05$). The IL-1β levels decreased only in the FMD group ($p < 0.05$), whereas no changes were found in IL-17 levels in any group. The levels of five out of six bacterial species decreased at 3 and/or 6 months only in the FMD group ($p < 0.05$).

Conclusions: The FMD treatment appears to offer superior outcome than Q-SRP and could be the first choice for patients with GAgP.

KEYWORDS
aggressive periodontitis, bacteria, interleukin-1 beta, interleukin-17, periodontal debridement

1 | INTRODUCTION

Generalized aggressive periodontitis (GAgP), is characterized by generalized severe destruction of tooth-supporting tissues in otherwise healthy individuals.[1] It is currently termed as stage III or IV and grade C in the new classification, which is based on a multidimensional staging and grading system and allows clinicians to incorporate individual patient factors into the diagnosis that are of great importance to detailed case management.[2,3] Standard periodontal treatment contains conventional quadrant-based scaling and root planing (Q-SRP), occasionally with adjunctive local or systemic antimicrobials such as antiseptics and antibiotics.[4–7] However, the common use of

antibiotics in various infections has raised concern for increased antimicrobial resistance. The resistance and poor patient compliance result in prolonged illnesses with the risk of emerging untreatable infectious diseases and greater risk of death.[8,9] Moreover, as stated in the recent Clinical Practice Guideline (CPG) for the treatment of Stage I–III periodontitis, routine use of systemic antibiotics as adjunct to subgingival instrumentation should not be recommended.[10] In periodontology, alternative non-surgical periodontal treatment (NSPT) approaches are sought to suppress bacterial re- and cross-infection from periodontal pockets and other oral sites.[11–13] Both full-mouth disinfection (FMD)[14] and full-mouth scaling and root planing (FM-SRP)[15] contain conventional mechanical treatment given within a single day, but FMD also incorporates whole-mouth chlorhexidine (CHX) applications. A successful periodontal therapy should lead to long-term clinical improvement together with decreased load of periodontitis-associated microbiota and re-established host-compatible periodontal ecosystem.[16,17]

Despite the reports of better clinical and microbiological outcomes after FMD than the traditional Q-SRP in patients with chronic periodontitis (CP),[11,12,18,19] recent systematic reviews stated that Q-SRP and the full-mouth debridement methods are all effective for the therapy of CP,[20,21] and that FMD provides additional benefit over Q-SRP in probing depth (PD) reduction and clinical attachment level (CAL) gain.[20] Furthermore, rigorous evidence-based CPG for the treatment of Stage I–III periodontitis confirmed that no substantial differences were observed between Q-SRP and FM-SRP protocols.[10] However, since FMD studies were not included in the analysis, no information was presented about the FMD performance in this CPG.[10] Regarding the patients with GAgP, most studies have used only one of the NSPT approaches.[13,22–27] Some of the few comparative studies available have revealed significant additional improvements in clinical parameters and/or in periodontopathogen levels in FMD over the Q-SRP strategy,[11,12] whereas some others found no difference in clinical parameters between FM-SRP and Q-SRP or they lack microbiological information.[28]

Extensive literature links certain bacterial species to AgP.[29] Although these species are also found on soft oral surfaces, their particular niche is in the subgingival area and their removal/suppression by instrumentation is therefore difficult. Since they belong to the normal oral microbiome, a mere detection of these species may not be as important as their amount.[30] During the past decade, quantitative PCR (qPCR) has been rather commonly used for bacterial analysis in periodontal studies, but none have compared the effect of three different NSPT modalities in GAgP patients.

Cytokines play a crucial role in the initiation and progression of periodontitis.[31] Interleukin (IL)-1β is a key pro-inflammatory mediator, also important in bone resorption and periodontal breakdown.[32,33] In terms of treatment results, most authors have reported reduction in IL-1β levels[24,34,35] and a few found no change.[36,37] IL-17 is a pro-inflammatory cytokine related to the pathogenesis of inflammation and autoimmunity as well as host defence against pathogens.[38,39] Since it participates in a series of biochemical pathways boosting inflammation and bone resorption,[40,41] IL-17 may play a crucial role in patients with severe periodontal destruction and functional impairment of polymorphonuclear leukocytes. Moreover, it induces the production of many cytokines such as IL-1β, tumour necrosis factor (TNF)-α, IL-6 and IL-8.[42,43] Alike IL-1β, limited and inconsistent data are available on IL-17 levels in GCF following NSPT strategies, revealing significant post-treatment reduction,[44] increase[34] or no change.[36] To our knowledge, there is no study available, comparing cytokine levels in patients with GAgP treated with different NSPT modalities.

In the present study, it was hypothesized that FMD consisting of an intensive antimicrobial regime with CHX and short-term NSPT will provide more favourable anti-inflammatory responses than other non-surgical treatment strategies. Therefore, the aim of the study was to compare the effects of Q-SRP, FMD and FM-SRP on clinical, biochemical and microbiological parameters in patients with GAgP.

2 | MATERIALS AND METHODS

2.1 | Study design and sample size calculation

The present study was designed as a 6-month prospective, examiner blind, randomized, controlled clinical trial (RCT). This study was carried out in accordance with the Helsinki Declaration of 1975, as revised 2013 after approval of the study design by the Yeditepe University Clinical Research Ethics Committee (protocol no: 257/13.11.2012). All patients were informed about the objectives, methods and potential risks and benefits of their participation in respective RCT and signed informed consent forms. The study protocol was registered at clinicaltrials.gov with the number NCT02466646 in June 2015.

Sample size was calculated based on the primary outcome, PD reduction in sites with PD > 6 mm. A previous study[45] reported a mean difference of 1.65 mm PD reduction between treatment groups for an expected standard deviation of 1.25 mm. Based on these data, 12 subjects for each group were required to detect a difference with power of 90% and an α error of 0.05. Fourteen patients per treatment group were included for any possible dropouts during the study.

2.2 | Patient screening, selection and randomization

Eighty-four patients diagnosed with GAgP[1] were assessed for eligibility by a clinician (DM) referred to the Clinics of Periodontology Department, Faculty of Dentistry, Marmara University between December 2012 and September 2014. Forty-two patients (25 females and 17 males) met the inclusion criteria and volunteered to participate in the study. The patients had at least four interdental sites with CAL of 5 mm or more in at least 30% of the teeth, at least three of the affected teeth not being first molars and incisors.

According to new periodontitis classification system,[2] all patients fulfilled the categorization of generalized stage-III and grade-C periodontitis in the point of the extent and severity. For entering the study, the patients met the following criteria: (1) having at least 20 teeth (excluding third molars), (2) no history of systemic conditions modifying the treatment outcome of periodontal treatment, (3) no smoking, (4) no periodontal treatment nor use of antibiotics in the past 6 months, (5) no pregnancy, and (6) no lactation.

Patients were randomly allocated into three groups according to a computer-generated randomization list (www.randomizer.org/Copyright© 1997–2020 by Geoffrey C. Urbaniak and Scott Plous) by a clinician (LK) after baseline examination. The three treatment strategies comprised Q-SRP, FMD and FM-SRP. Patients and the clinician (DM) who conducted the treatment were not blinded due to the design and nature of the study. Figure 1 shows a consort flow diagram of progress through the phases of the present RCT.

2.3 | Clinical measurements

Clinical examinations were performed as previously reported[46] at baseline, 3 and 6 months after treatment by a single calibrated examiner (BD) who was blinded to all groups. Intra-examiner calibration was carried out in five similar periodontitis patients not included in the study. Pairs of PD and CAL measurements were recorded with 1-day interval. The intraclass correlation was 0.93 for

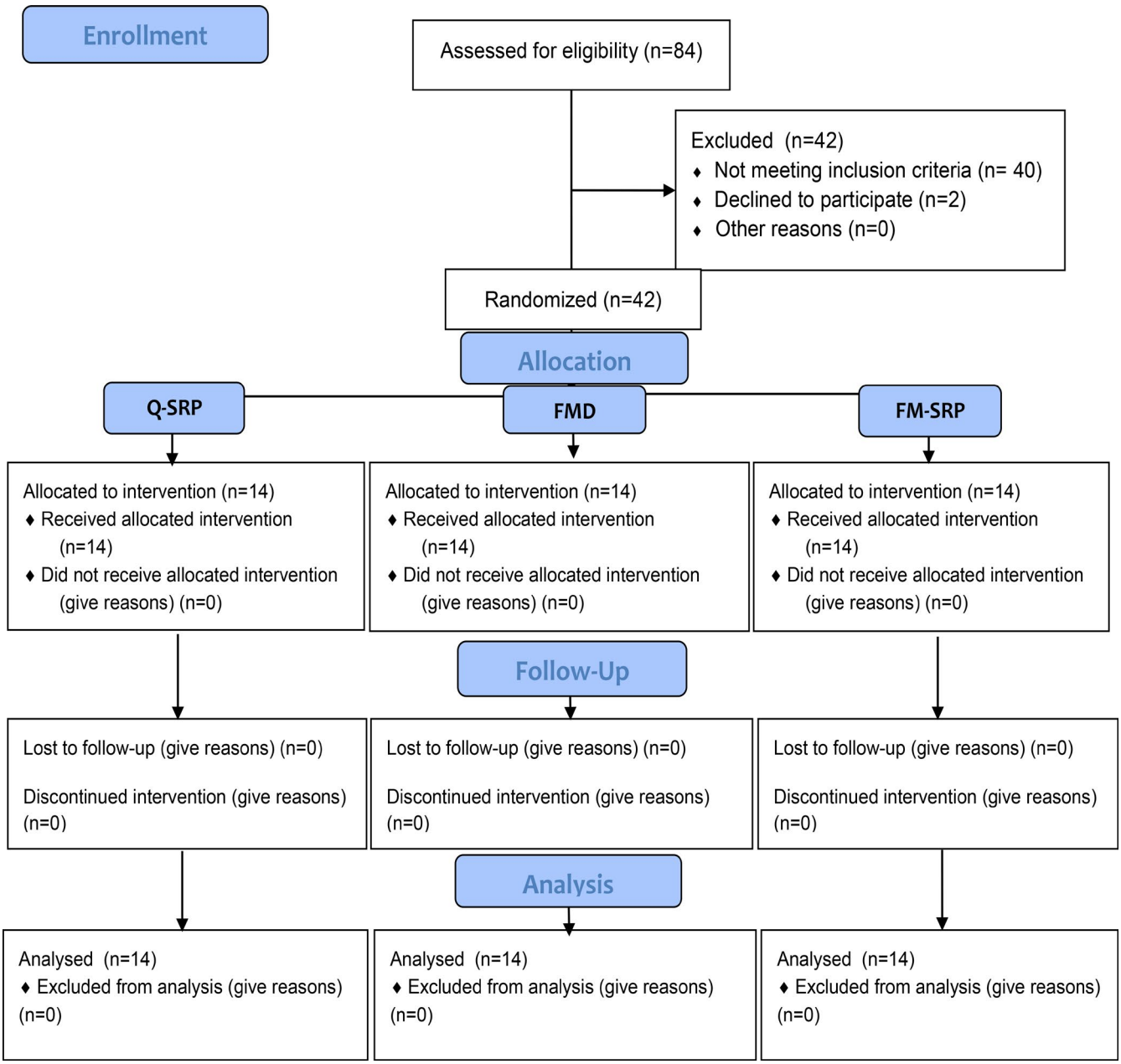

FIGURE 1 Flow diagram showing the study design

PD and 0.91 for CAL. Clinical periodontal measurements including plaque index (PI),[47] gingival index (GI),[48] bleeding on probing (BOP), PD and CAL were taken at six sites per tooth (mesio-buccal, buccal, disto-buccal, mesio-lingual, lingual and disto-lingual) in all teeth, except third molars. PD and CAL were measured using a University of North Carolina 15 periodontal probe (Hu-Friedy). The primary outcome variable of the study was PD reduction in sites PD > 6 mm and the secondary outcomes percentage of pocket closure, CAL and BOP.

2.4 | Treatment procedures

NSPT was performed under local anaesthesia by a clinician (DM) using periodontal curettes (5/6, 11/12, 13/14 Gracey curettes, Hu-Friedy) and ultrasonic device (Bobcat Pro 25K Ultrasonic Scaler, Dentsply Professional). All patients had received oral hygiene instructions on brushing, flossing and/or interdental brushing before periodontal treatment.

In the Q-SRP group, SRP was performed quadrant by quadrant with 1-week interval in a total of four sessions[49] and in the FM-SRP group in two sessions within 24 h.[15] In the FMD group, SRP was completed in 2 sessions within 24 h and immediately after each instrumentation session, additional disinfection was carried out consisting of brushing the tongue with a 1% CHX gel (Klorhex 1% gel, Drogsan) for 1 min, rinsing twice with a 0.2% CHX solution (Klorhex 0.2% solution, Drogsan) for 1 min, spraying the tonsils with a 0.2% CHX spray (Klorhex 0.2% spray, Drogsan) and subgingival irrigation of all pockets 3 times within 10 min with 1% CHX gel using a syringe with a blunted needle tip. Subgingival CHX irrigation was repeated at day 8. FMD protocol continued by rinsing with 0.2% CHX solution for 1 min and spraying the tonsils with 0.2% CHX spray twice daily during 3 weeks after periodontal treatment.[14]

Oral hygiene of all patients was reviewed, and oral hygiene procedures were reinforced with 2-week intervals in the first 3 months and with 4-week intervals in the subsequent 3 months. At these recall visits, supragingival scaling and polishing were performed if necessary. However, no subgingival instrumentation was performed until the end of the study in order not to interfere with subgingival microbiota.

2.5 | GCF and microbiological sampling

Buccal aspects of eight interproximal subgingival sites, one single-rooted and one multi-rooted tooth with PD ≥ 5 mm from each quadrant per patient were chosen for GCF and microbiological samplings. The samples were collected and pooled from the same sites at baseline, 3 and 6 months after treatment. For GCF sampling, the selected teeth were isolated by cotton rolls and their surfaces were dried, and then, the supragingival plaque was removed using sterile cotton pellets. The GCF samples were collected, as previously described.[50] Paper strips (Periopaper, Oraflow Inc.) were inserted 1–2 mm to the periodontal pockets for 30 s. Strips contaminated with blood were discarded. The sample volume was measured using a calibrated device (Periotron 8000, Proflow Inc.), and the reading was converted to the actual volume (μl) by reference to the standard curve. Following GCF sampling, the subgingival plaque samples were obtained from the same periodontal sites, as previously reported.[51] Briefly, a sterile paper point (No. 30, Meta Absorbent Paper points; MetaBiomed Co., Ltd.) was inserted into each subgingival site for 10 s. The paper points were then pooled into a single empty sterile eppendorf tube and immediately placed at −80°C, where they were preserved until sent to Oral Microbiology, Research Laboratory, Faculty of Dentistry, Kuwait University, by express mail delivery to be used for further analysis. All GCF and microbiological samples were analysed together at the end of the clinical phase of the study.

The researchers who carried out the biochemical (LK) or microbiological (MK) analyses were blinded to the clinical groups during the laboratory procedures.

2.6 | Biochemical analyses

Pooled GCF samples were eluted and analysed by ELISA using commercially available kits for IL-1β (HS, Quantikine; R&D Systems Inc.) and IL-17 (Quantikine; R&D Systems Inc.) at Biochemistry Laboratory, Faculty of Dentistry, Marmara University, as previously reported.[52] Assays were carried out according to the manufacturer's recommendations using human recombinant standards, and the optical density was measured at 450 or 490 nm. The results were reported as total amount (picogram) for both cytokines. The minimum detection limits in the assays were 0.057 pg/ml for IL-1β and 15 pg/ml for IL-17. The cytokine levels exceeded detection levels in all eluted GCF samples.

2.7 | qPCR

Species-specific 16S rRNA gene primers from published literature were chosen and revalidated in silico in our laboratory in our earlier study.[53] All qPCR reactions were carried out using Power SYBR Green® Kit on a Real-Time PCR machine ABI 7500 Fast (Applied Biosystems). Temperature profile consisted of 40 cycles of denaturation at 95°C for 15 s, annealing at 50°C–56°C for 30 s (depending on the primer pair) and extension at 72°C for 30 s. Serial dilutions of genomic DNA from the reference species *Aggregatibacter actinomycetemcomitans* SA269, *Porphyromonas gingivalis* ATCC 33277, *Fusobacterium nucleatum* ssp. *polymorphum* NCTC 10562, *Parvimonas micra* CCUG 46357, *Prevotella intermedia* ATCC 25611 and *Campylobacter rectus* UMEA-12 were used in each reaction. For each bacterium, qPCR was studied in double and the mean values were used. The Ct values were plotted against bacterial cell concentration (CFU/ml) of each species to generate a standard curve. Bacterial cell quantities below the detection limit of 100 cells/ml were regarded as zero.

2.8 | Statistical analysis

Data were analysed by SPSS version 20.0 (SPSS, IBM). The clinical, biochemical and microbiological data were expressed as median (Q1–Q3) values. PD measurements were also categorized as sites with moderate (PD = 4–6 mm) and deep (PD > 6 mm) pockets, and their percentages of all PDs and proportion of 'pocket closure' (PD ≤ 3 mm) were computed for each patient. In addition, percentages of sites with both PD ≥ 5 mm and BOP were calculated and designated as residual pockets at post-treatment visits.

Multiple comparisons of the clinical, biochemical and microbiological parameters among groups were performed using Kruskal–Wallis test. When significance occurred, Bonferroni-corrected Mann–Whitney *U*-test was used for paired comparisons. Within groups, multiple comparisons at different time points were performed using Friedman test and pairwise comparison by the Bonferroni-corrected Wilcoxon signed-rank test. The correlations among clinical, biochemical and microbiological parameters before and after treatment were determined by Spearman-correlation analysis. Chi-squared test was used to compare gender distribution among groups. Statistical significance was set at an α level of <0.05.

3 | RESULTS

There were no dropouts throughout the study period. None of the patients had any adverse reaction during the study. Moreover, after 3-week follow-up, no difference was observed in the home care regimen among patients.

3.1 | Clinical measurements

Table 1 shows intra- and inter-group comparisons of the median (Q1-Q3) values of all clinical periodontal parameters at baseline, 3 and 6 months. No differences were found among treatment groups at baseline ($p > 0.05$). In all treatment groups, full-mouth PI, GI, BOP, PD and CAL, and the percentages of moderate and deep pockets improved significantly from their respective baseline values ($p < 0.05$). Values of BOP and percentages of moderate, deep and residual pockets were significantly lower for the FMD group compared with Q-SRP ($p < 0.05$). Although full-mouth PD was significantly higher in Q-SRP compared with FMD after treatment ($p < 0.05$), it was below 4 mm in all treatment groups. Full-mouth PD and CAL reductions from baseline to 6 months were similar among treatment groups ($p > 0.05$). FMD also produced significantly improved results over FM-SRP for PI and percentages of moderate pockets and pockets with PD ≥ 5 mm and BOP ($p < 0.05$).

Table 2 shows intra- and inter-group comparisons of PD values (mm) obtained from pockets initially categorized as moderate, deep and sampled sites, and of PD reduction (mm) and CAL gain (mm) from baseline to 6 months. In all treatment groups, the PD values of all pocket categories were lower at 3 and 6 months than respective baseline values ($p < 0.05$). At 6 months, FMD resulted in lower PD values of initially moderate pockets than Q-SRP ($p < 0.05$) and of initially deep pockets at 3 and 6 months ($p < 0.05$). PD reduction was greater in FMD than Q-SRP group in initially moderate pockets ($p < 0.05$). The PD reduction and CAL gain of initially deep pockets and sampled sites were greater in FMD than Q-SRP group ($p < 0.05$). Only PD reduction was greater in FM-SRP than Q-SRP group.

The proportion of sites reaching the successful treatment endpoint of pocket closure at 3 and 6 months is presented in Table 3. Percentage of the pocket closure (PD ≤ 3 mm) in sites with PD = 4–6 mm both at 3 and 6 months was significantly higher in FMD group compared with Q-SRP and FM-SRP groups ($p < 0.05$). Moreover, in sites with PD > 6 mm, FMD showed significantly more closed pockets compared with Q-SRP at both time points. Percentage of overall pocket closure in diseased sites (PD > 4 mm) at 3 and 6 months in Q-SRP (41.9% and 43.9%, respectively) and in FM-SRP (53% and 50.4%, respectively) was significantly lower than FMD (73.2% and 69.8%, respectively; $p < 0.05$).

3.2 | Biochemical results

Figure 2 shows that the total amount of IL-1β in GCF decreased significantly only in the FMD group ($p < 0.05$). No inter-group differences were observed ($p > 0.05$; Panel A).

Regarding IL-17, no inter- or intra-group differences were found at any time point ($p > 0.05$; Panel B).

GCF volume significantly decreased from baseline in all treatment groups at 3 and 6 months ($p < 0.05$), while there were no inter-group differences at any time point ($p > 0.05$; Panel C).

Correlation analysis results between selected study variables of 42 patients at baseline and at 6 months are demonstrated in Table 4. IL-1β levels correlated positively with PD at sampled sites ($r = 0.357$, $p < 0.05$) at baseline. No such correlations were seen at 6 months.

GCF volume correlated positively with *A. actinomycetemcomitans* counts ($r = 0.324$, $p < 0.05$) at 6 months.

3.3 | Microbiological results

A. actinomycetemcomitans correlated positively with *P. gingivalis* ($r = 0.326$, $p < 0.05$) at baseline, while all other species with each other at both baseline and 6 months after treatment ($p < 0.01$) (Table 4). *P. gingivalis* correlated significantly with both whole-mouth and sampled sites PD at baseline and with *P. intermedia* ($p < 0.05$ for all) at 6 months, whereas *C. rectus* with sampled pockets at baseline ($r = 0.324$, $p < 0.05$). Positive correlations were also detected for *P. gingivalis* with CAL ($r = 0.346$, $p < 0.05$) and for *P. intermedia* with PI at baseline ($r = 0.335$, $p < 0.05$), while at 6 months for *F. nucleatum* and *P. micra* with PI ($r = 0.553$, $p < 0.01$ and $r = 0.374$, $p < 0.05$, respectively) and *A. actinomycetemcomitans* with the GCF volume ($r = 0.324$, $p < 0.05$).

TABLE 1 Comparison of age, gender and clinical parameters among treatment groups at baseline, 3 and 6 months

Clinical parameters	Time points	GROUPS (A) Q-SRP N = 14	(B) FMD N = 14	(C) FM-SRP N = 14	(A-B-C) p^a	(A-B) p^b	(B-C) p^b	(A-C) p^b
Age (years)		30.5 (25.5–35.5)	26.0 (20.8–30.8)	32.5 (28–35.5)	0.072			
Gender [male *N* (%)]		7 (50)	4 (29)	6 (43)	0.501			
PI	Baseline	1.9 (1.5–2.0)	1.5 (1.3–1.6)	1.6 (1.5–1.8)	0.074	1.000	**0.010**	0.050
	3 months	0.7*(0.5–0.9)	0.7*(0.6–0.8)	0.9*(0.8–1.0)	**0.008**			
	6 months	0.7*(0.7–1.0)	0.7*(0.6–0.8)	0.8*(0.7–0.1)	0.373			
	p^c	**<0.001**	**<0.001**	**<0.001**				
GI	Baseline	1.9 (1.6–2.0)	1.5 (1.4–1.8)	1.8 (1.6–1.9)	0.093			
	3 months	1.1*(0.9–1.4)	1.2*(1.1–1.3)	1.2*(1.2–1.3)	0.295			
	6 months	1.3*(1.1–1.4)	1.2*(1.2–1.3)	1.2*(1.1–1.3)	0.528			
	p^c	**<0.001**	**<0.001**	**<0.001**				
BOP (%)	Baseline	91.7 (80.3–97.2)	82.7 (63.6–89.1)	90.8 (74.7–95.8)	0.141			
	3 months	51.8*(43.8–65.4)	39.1*(33.0–45.5)	44.4*(42.2–57.4)	**0.005**	**0.005**	0.069	1.000
	6 months	59.9*(48.6–76.0)	43.6*(38.5–47.7)	53.3*(35.2–60.7)	**0.006**	**0.004**	0.376	0.284
	p^c	**<0.001**	**<0.001**	**<0.001**				
PD (mm)	Baseline	5.1 (4.2–5.3)	4.8 (4.0–5.0)	4.8 (4.3–5.4)	0.383			
	3 months	3.2*(2.9–3.5)	2.8*(2.4–3.0)	3.0*(2.7–3.3)	**0.008**	**0.007**	0.146	0.822
	6 months	3.3*(3.1–3.6)	2.8* (2.4–3.0)	3.1*(2.8–3.3)	**<0.001**	**<0.001**	0.069	0.283
	p^c	**<0.001**	**<0.001**	**<0.001**				
PD reduction	0–6 months	1.2 (0.7–2.8)	1.9 (0.9–2.9)	1.8 (1.3–2.9)	0.076			
PD = 4–6 mm (%)	Baseline	40.5 (34.8–51.8)	43.0 (34.5–55.3)	47.5 (31.8–53.3)	0.891			
	3 months	29.0*(20.5–40.0)	17.5*(8.0–25.5)	28.5*(24.0–37.0)	**0.003**	**0.007**	**0.014**	1.000
	6 months	34.0 (24.5–36.8)	18.5*(10.5–25.5)	28.5*(22.8–36.0)	**0.008**	**0.008**	0.087	1.000
	p^c	**0.021**	**<0.001**	**<0.001**				
PD > 6 mm (%)	Baseline	23.5 (13.3–32.0)	19.0 (10.8–30.3)	21.0 (15.3–33.3)	0.615			
	3 months	3.5*(1–5.0)	1.0*(0–2.0)	1.5*(0–3.0)	**0.004**	**0.003**	0.493	0.178
	6 months	3.0*(1–8.5)	1.0*(0–1.3)	2.0*(0–2.5)	**0.020**	**0.015**	0.625	0.369
	p^c	**<0.001**	**<0.001**	**<0.001**				
PD ≥ 5 mm and BOP + (%)	Baseline	53.9 (43.3–65.7)	44 (38.1–59.6)	58.0 (42.6–65.5)	0.250			
	3 months	15.5* (9.2–21.2)	4.8* (1.1–8.0)	10.5* (8.1–15.2)	**<0.001**	**<0.001**	**0.007**	0.832
	6 months	16.7* (10.4–21.3)	5.3* (1.6–7.5)	10.8* (5.8–15.4)	**<0.001**	**<0.001**	0.090	0.126
	p^c	**<0.001**	**<0.001**	**<0.001**				

TABLE 1 (Continued)

Clinical parameters	Time points	GROUPS (A) Q-SRP N = 14	(B) FMD N = 14	(C) FM-SRP N = 14	(A-B-C) p^a	(A-B) p^b	(B-C) p^b	(A-C) p^b
CAL (mm)	Baseline	5.5 (4.5–6.7)	5.3 (4.5–6.1)	5.9 (5.2–6.3)	0.276			
	3 months	4.4*(4.0–5.3)	4.7*(4.1–5.1)	4.9*(4.5–5.7)	0.215			
	6 months	4.5*(4.2–5.6)	4.5*(4.2–5.1)	4.9*(4.6–5.8)	0.164			
	p^c	**0.040**	**0.002**	**<0.001**				
CAL gain	0–6 months	0.6 (1.2–1.4)	0.8 (0.4–1.0)	0.7 (0.2–1.1)	0.964			

Note: Data are presented as median (Q1–Q3) values, except for gender in number (%) of patients. Statistically significant differences are marked with boldface text. *Significant difference from baseline (Bonferroni-corrected Wilcoxon signed-rank test), $p < 0.05$.

Abbreviations: BOP, bleeding on probing; CAL, clinical attachment level; FMD, full-mouth disinfection; FM-SRP, full-mouth-based scaling and root planing; GI, gingival index; PD, probing depth; PI, plaque index; Q-SRP, quadrant-based scaling and root planing.

[a]for gender: Chi-squared test; others: Kruskal–Wallis test.

[b]Bonferroni-corrected Mann–Whitney *U*-test.

[c]Friedman test.

Table 5 demonstrates comparisons of microbiological results for treatment groups. The test species were prevalent at baseline and only small post-treatment changes were seen in their detection rates. The total counts of test species did not differ between treatment groups at baseline. At 3 months, their total counts were lower in the FMD than FM-SRP group ($p < 0.05$). Excluding *P. gingivalis*, the amounts of individual test species significantly decreased during the 6-month study period in the FMD group, the levels of *P. gingivalis*, *F. nucleatum*, *P. intermedia* and *C. rectus* in the Q-SRP group ($p < 0.05$), but only of *P. gingivalis* in the FM-SRP ($p < 0.05$) group. The only significant difference between the treatment groups was the lower level of *P. intermedia* in FMD compared with Q-SRP at 3 months ($p < 0.05$).

Figure 3 shows line charts for the test species per patient in each treatment group at baseline, 3 and 6 months. A wide individual variation in the post-treatment counts was particularly evident for *A. actinomycetemcomitans*, *P. gingivalis* and *P. intermedia*. In contrast, amounts of *F. nucleatum*, *P. micra* and *C. rectus* were more clustered in all treatment groups, as seen for their representative, *C. rectus*.

4 | DISCUSSION

Since the 1999 Workshop on Classification of Periodontal Diseases and Conditions,[1] substantial new information has been revealed from population-based studies, basic science investigations and the evidence from prospective studies regarding to GAgP.[54,55] The analysis of those information revealed significant heterogeneity in the diagnosis criteria and definition of GAgP. Therefore, the new classification system for periodontitis including staging and grading system was introduced to overcome these problems.[2,56] As the present study was conducted between 2012 and 2014, included patients were diagnosed with GAgP, according to 1999 classification system.[1] When the new classification system was presented in 2018, the authors preciously re-evaluated all clinical and radiographic data of the patients, reclassified according to the new classification system and revealed that all patients fully met the generalized stage-III and grade-C periodontitis feature. However, using the term 'GAgP' was preferred to keep on as the results of the present study were also compared with previous GAgP studies.

The present RCT on patients with GAgP compared clinical, biochemical and microbiological results of three NSPT strategies, Q-SRP, FMD and FM-SRP. It is well known that full-mouth strategies shorten the number sessions on dental chair and duration of NSPT.[14] The shorter working duration restricts the risk of cross-contamination between treated and untreated sites, thereby, allowing better control of the transmission of periodontopathogens between the bacterial niches.[15] Moreover, with FMD, the number of sessions is reduced but the sessions are longer which may cause fatigue of the clinician or the patient. However, during the present study, no patient or clinician (DM) complaints were reported in full-mouth strategies groups.

TABLE 2 Inter- and intra-comparison of median (Q1-Q3) PD and CAL gain values at sites initially PD 4–6 mm and >6 mm and at sampled sites initially PD ≥ 5 mm

			GROUPS						
Clinical parameters		**Time points**	**(A) Q-SRP $N = 14$**	**(B) FMD $N = 14$**	**(C) FM-SRP $N = 14$**	**(A-B-C) p^a**	**(A-B) p^b**	**(B-C) p^b**	**(A-C) p^b**
Initially PD = 4–6 mm	PD (mm)	Baseline	5 (4.9–5.2)	5 (4.8–5.1)	5 (5–5.2)	0.051			
		3 months	3.3*(2.6–4.3)	2.8*(2.3–3.5)	3.2*(2.7–5.2)	0.052			
		6 months	3.4*(2.7–4.6)	2.8*(2.3–3.5)	3.2*(2.6–3.5)	**0.001**	**0.001**	0.102	0.322
		p^c	**<0.001**	**<0.001**	**<0.001**				
	PD reduction	0–6 months	1.5 (1.2–1.9)	2.2 (1.7–2.5)	1.8 (1.7–2.3)	**0.014**	**0.017**	1.000	0.078
	CAL gain	0–6 months	0.4 (0.2–1.2)	1 (0.7–1.3)	0.6 (0.4–1)	0.152			
Initially PD > 6 mm	PD(mm)	Baseline	7.8 (7.4–8.5)	7.7 (7–8.7)	7.7 (7.3–9)	0.746			
		3 months	4.9*(3.5–7)	4*(2.8–5.6)	4.6*(3.3–5.2)	**0.005**	**0.003**	0.141	0.611
		6 months	5.1*(3.9–6.6)	4*(2.8–4.8)	4.5*(3–5)	**0.001**	**<0.001**	0.222	0.117
		p^c	**<0.001**	**<0.001**	**<0.001**				
	PD reduction	0–6 months	2.8 (2.2–3.2)	3.7 (3–4.2)	3.6 (2.8–4)	**0.007**	**0.010**	1.000	**0.040**
	CAL gain	0–6 months	1.5 (1.1–1.8)	2.3 (2–2.6)	2.2 (1.4–2.7)	**0.007**	**0.007**	1.000	0.095
Sampled sites initially PD ≥ 5 mm	PD(mm)	Baseline	6.7 (6.1–7.2)	6.2 (5.8–7.4)	6.5 (5.9–7.0)	0.642			
		3 months	4.3*(3.8–4.9)	3.3*(3–3.7)	3.8*(3.4–4.2)	**0.001**	**0.001**	0.115	0.309
		6 months	4.3*(3.9–5.0)	3.3*(3.1–3.7)	3.8*(3.4–4.5)	**<0.001**	**<0.001**	0.053	0.310
		p^c	**<0.001**	**<0.001**	**<0.001**				
	PD reduction	0–6 months	2.2 (1.9–2.9)	3.1 (2.5–3.8)	2.6 (1.9–3.1)	**0.027**	**0.022**	0.819	0.341
	CAL gain	0–6 months	0.9 (0.3–1.6)	1.6 (1.3–2.2)	1.4 (0.8–2.1)	**0.028**	**0.023**	0.830	0.346

Note: Statistically significant differences are marked with boldface text.

*Significant difference compared with baseline (Bonferroni-corrected Wilcoxon signed-rank test), $p < 0.05$.

Abbreviations: CAL, clinical attachment level; FMD, full-mouth disinfection; FM-SRP, full-mouth-based scaling and root planing; PD, probing depth; Q-SRP, quadrant-based scaling and root planing.

[a]Kruskal–Wallis test.

[b]Bonferroni-corrected Mann–Whitney *U*-test.

[c]Friedman test.

TABLE 3 Inter- and intra-comparison of percentage of pocket closure (PD ≤ 3 mm) at sites initially PD = 4–6 mm, PD > 6 mm and at whole mouth among treatment groups

Clinical parameters	Time points	GROUPS (A) Q-SRP N = 14	(B) FMD N = 14	(C) FM-SRP N = 14	(A-B-C) p^a	(A-B) p^b	(B-C) p^b	(A-C) p^b
% of closed pockets initially PD = 4–6 mm	3 months	60.9 (43.1–88.1)	86.4 (80.5–92.4)	71.5 (60.6–79.5)	**0.008**	**0.016**	**0.030**	1.000
	6 months	62 (44.4–70.3)	86 (73.9–91.1)	64.1 (57.4–75.2)	**0.001**	**0.001**	**0.021**	1.000
	p^c	0.198	0.221	0.594				
% of closed pockets initially PD > 6 mm	3 months	18.7 (3.2–36.8)	43 (30.1–52.5)	23.6 (12.2–37.1)	**0.024**	**0.029**	0.116	1.000
	6 months	15.7 (5.4–26.3)	35.5 (25–55.1)	25 (11.1–48.3)	**0.009**	**0.006**	0.441	0.306
	p^c	0.203	0.414	0.308				
Total % of closed pockets initially PD > 3 mm	3 months	41.9 (32.1–67.8)	73.2 (64.3–83)	53 (45.7–61.5)	**0.001**	**0.001**	**0.012**	1.000
	6 months	43.8 (32.6–53.9)	69.8 (61.4–78)	50.4 (44.9–63.4)	**<0.001**	**<0.001**	**0.018**	0.370
	p^c	0.300	0.331	0.754				

Note: Data are presented as median (Q1-Q3). Statistically significant differences are marked with boldface text.

Abbreviations: FMD, full-mouth disinfection; FM-SRP, full-mouth-based scaling and root planing; PD, probing depth; Q-SRP, quadrant-based scaling and root planing.

[a]Kruskal–Wallis test.

[b]Bonferroni-corrected Mann–Whitney U-test.

[c]Wilcoxon signed-rank test, $p < 0.05$.

It appeared that at baseline, there were no statistically significant differences between the treatment groups. All treatment strategies, particularly FMD, improved clinical variables and decreased levels of most tested bacteria and IL-1β. The 6-month study period was chosen, since previous studies reported that GAgP responds well to NSPT up to 6 months.[26,28] Studies with longer follow-up showed that after 6 months, PD increase and clinical attachment gain starts to decrease[57,58] This may be explained by the presence of residual pockets which harbour bacterial species correlated with periodontal diseases and capable of determining a new periodontal breakdown and represent true risk factors for both periodontal disease progression and tooth loss.[59]

Subjects in FMD group showed significantly less sites with BOP and lower full-mouth PD compared with Q-SRP group after treatment. However, all treatment strategies showed similar effect in full-mouth reduction in both PD and CAL values. The full-mouth PD provides a general picture of the mouth since it consists of shallow, moderate and deep pockets. In the present study, 1/3 of the sites were shallow and did not show considerable changes in PD and CAL after treatment which may mask the main improvement in moderate and deep sites.[9] To overcome this problem, further analyses were performed based on different PD categories. The clinical significant benefits of FMD were observed in both moderate (4–6 mm) and especially deep PD (>6 mm) sites by providing additional 0.70 mm PD reduction in moderate pockets and, 0.9 mm PD reduction and 0.8 mm CAL gain in deep pockets versus the Q-SRP. It is in accordance with earlier findings of studies regarding early-onset periodontitis or CP.[12] Since additional benefits were observed especially in deep pockets in favour of FMD versus Q-SRP, FMD can be preferable in severe periodontitis patients with high risk for cross-contamination.

An expected endpoint of non-surgical treatment should include sites reaching the successful pocket closure.[21] In the current study, the overall pocket closure reached to 73% in FMD but 42% in Q-SRP ($p < 0.05$) and 53% in FM-SRP ($p < 0.05$) at 3 months and maintained at 6 months. Results in pocket closure between Q-SRP and FM-SRP groups are in accordance with a recent systematic review.[21] However, this is the first study, which evaluates FMD for pocket closure in GAgP patients.

In this study, percentage of residual pockets significantly decreased at 3 months compared with baseline in all treatment strategies and maintained at 6 months. These findings were in accordance with previous studies.[23,24,26,60] Furthermore, the percentage of residual pockets was significantly lower after FMD than FM-SRP or Q-SRP at 3 months, but only Q-SRP at 6 months. To date, there are no other studies available to enable comparisons between the respective results. The superiority of FMD, resulting in PD reduction and decreased proportion of residual pockets, is important for further treatment planning in patients with GAgP. Well known is that clinical improvement leads to diminished subgingival space for the reestablishment of pathogenic microenvironment. Also, clinical findings have consistently shown that residual pockets are associated with future disease progression.[59,61]

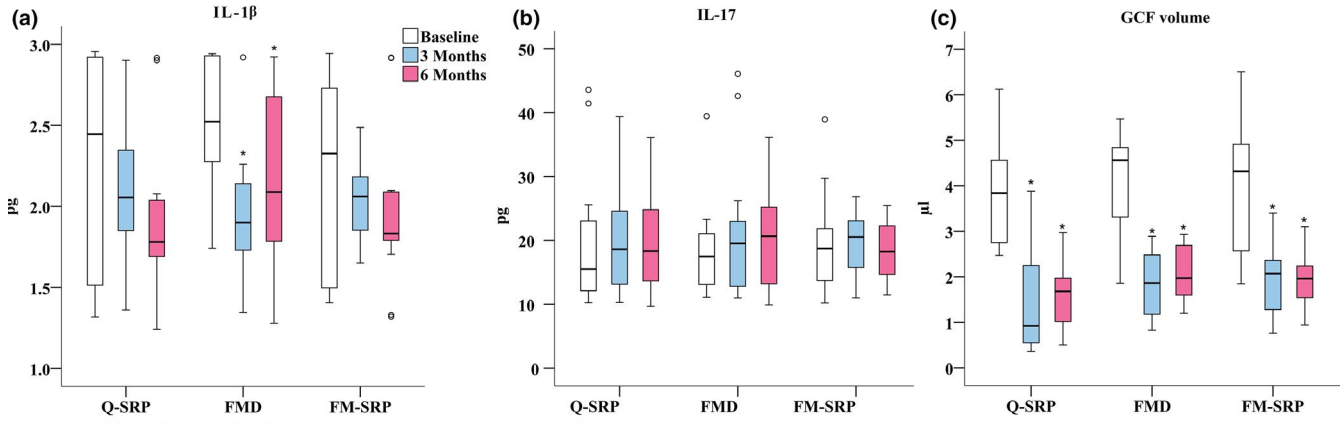

FIGURE 2 Box-and-whisker plots of changes in the amounts of IL-1β and IL-17 in gingival crevicular fluid and the volume of gingival crevicular fluid in three treatment groups. Panels A and B show the amounts of IL-1β (picogram) and IL-17 (picogram) in gingival crevicular fluid, and Panel C shows the volume (microliter) of gingival crevicular fluid. Boxes show the medians 25th (Q1) and 75th (Q3) percentiles, and whiskers show the 10th and 90th percentiles. Outliers are indicated by °. *Significant difference from baseline (Bonferroni-corrected Wilcoxon Signed-Rank Test, $p < 0.05$). Abbreviations: FMD, full-mouth disinfection; FM-SRP, full-mouth scaling and root planing; GCF, gingival crevicular fluid; IL, interleukin; pg, picogram; Q-SRP, quadrant-based scaling and root planing; µl, microliter. Colour codes depict examination time points

Periodontal disease activity is regulated by complex interactions between the host immune system and periodontal pathogens.[62] IL-1β and IL-17 are cytokines that enhance immune response against bacteria.[31] Moreover, IL-17 synergizes potently with IL-1β.[41] To find out how clinical variables relate to cytokine levels and subgingival microbiota in different NSPT strategies, both GCF and subgingival samples were consistently collected from the same sites at all visits. In most of the previous studies, GCF or microbiological samples were collected from 1 to 4 sites of the teeth, mostly single-rooted or deepest sites without information of root type of the tooth.[11,18,25,26,34,63,64] Since it is well known that multi-rooted teeth are difficult to access for instrumentation compared with single-rooted teeth, in this study pooled GCF and microbiological samples were collected from 8 sites, which were from one single- and one multi-rooted teeth of each quadrant, as a well representative of the whole mouth. IL-17 is a pro-inflammatory cytokine related to the pathogenesis of inflammation and autoimmunity as well as host defence against pathogens.[38,39] Increase levels of IL-1β in GCF samples of periodontitis patient have been well documented, and it plays a crucial role in the pathogenesis of periodontal tissue destruction.[31–33] Along with significantly lower post-treatment values for GCF volume, the IL-1β levels also decreased in all treatment groups, but significantly only in the FMD group. Several previous studies have also reported decreased IL-1β levels in GCF after SRP,[24,34,35,63] but no comparative studies were available. Furthermore, PD has significant impact on the local IL-1β levels.[65,66] In accordance with these findings, the present study showed that as the sampled sites PD increases periodontal inflammation enhances and as a result local IL-1β levels raised at baseline. Conversely, the GCF levels of IL-17 remained nearly the same in all treatment groups throughout our study period. This is in disagreement with one of the few studies on IL-17 in GAgP patients,[44,64] but partly agrees with another one that revealed no post-treatment change in the level of IL-17 at 3 months.[36] The discrepancies between the studies may result not only from different study designs, number of patients and sampled sites, but also individual differences in immune response.[67]

Based on previous literature, we chose counts of six bacterial species as surrogate markers for periodontopathogenic subgingival microecology. Our study showed that total tested bacteria counts were significantly lower in FMD compared with FM-SRP at 3 months. Moreover, FMD significantly decreased counts of most test species for 6 months as assessed by qPCR, but FM-SRP of one species only, even though both strategies applied a single-day full-mouth SRP. The possible explanation may be due to the use of meticulous CHX applications both by the clinician and patients which minimized the bacterial translocation, reduced subgingival regrowth and/or chance for reinfection. Only FMD decreased *A. actinomycetemcomitans* counts significantly, while both Q-SRP and FM-SRP decreased those of *P. gingivalis*. This confirms previous notions that decreasing *A. actinomycetemcomitans* levels may need adjunctive antimicrobials, but adequate SRP and biofilm control are enough to enhance reduction in *P. gingivalis*.[68]

No studies were encountered comparing microbiological results of the three NSPT strategies in GAgP patients. However, when two strategies, FMD and Q-SRP, were compared in patients with early-onset periodontitis, FMD provided more beneficial outcome as assessed by bacterial culture or checkerboard DNA-DNA hybridization.[11,18] This was interesting, since these bacteriological methods fundamentally differ from the qPCR technique we used. That our results agree with theirs support the ability of a single FMD session to produce favourable changes in subgingival microbiota for several months. However, worth remembering is that our test species are

TABLE 4 Correlations between selected clinical, biochemical and microbiological parameters in 42 patients at baseline and 6 months after treatment.

Baseline	*A. actinomycetemc.*	*P. gingivalis*	*F. nucleatum*	*P. micra*	*P. intermedia*	*C. rectus*	IL-1β (pg)	IL-17 (pg)	GCF (μl)
PI	0.064	0.094	0.199	0.200	0.335*	0.152	0.069	0.152	−0.211
GI	−0.005	0.016	0.110	0.155	0.251	0.083	0.055	0.175	−0.253
PD	0.136	0.480**	0.196	0.188	0.307*	0.286	0.185	0.016	0.012
CAL	0.192	0.346*	0.172	0.082	0.299	0.190	−0.138	0.078	−0.024
PD (mm) sampled sites	−0.090	0.378*	0.167	0.143	0.294	0.324*	0.357*	−0.136	0.222
PD ≥ 5 mm and BOP + (%)	0.164	0.368*	0.146	0.177	0.210	0.227	0.096	0.107	−0.043
A. actinomycetemcomitans	-	0.326*	0.093	0.293	0.093	0.232	−0.186	0.159	−0.119
P. gingivalis	0.326*	-	0.486**	0.504**	0.630**	0.741**	0.239	−0.243	−0.092
F. nucleatum	0.093	0.486**	-	0.532**	0.567**	0.727**	0.217	−0.035	0.017
P. micra	0.293	0.504**	0.532**	-	0.427**	0.680**	0.230	−0.065	−0.050
P. intermedia	0.093	0.630**	0.567**	0.427**	-	0.711**	0.148	−0.032	0.095
C. rectus	0.232	0.741**	0.727**	0.680**	0.711**	-	0.180	−0.026	0.073
IL−1β (pg)	−0.186	0.239	0.217	0.230	0.148	0.180	-	−0.297	0.257
IL−17 (pg)	0.159	−0.243	−0.035	−0.065	−0.032	−0.026	−0.297	-	−0.023
GCF (μl)	−0.119	−0.092	0.017	−0.050	0.095	0.073	0.257	−0.023	-
6 months									
PI	0.008	0.214	0.553**	0.374*	0.299	0.259	−0.005	0.023	0.224
GI	0.108	0.324*	0.380*	0.422**	0.305*	0.281	0.133	−0.112	0.291
PD	0.084	0.428**	0.289	0.243	0.500**	0.302	−0.051	−0.028	0.100
CAL	0.188	0.272	0.284	0.217	0.295	0.199	0.046	−0.014	0.231
PD (mm) sampled sites	−0.028	0.273	0.183	0.184	0.324*	0.156	−0.195	−0.060	−0.049
PD ≥ 5 mm and BOP + (%)	0.141	0.513**	0.216	0.273	0.444**	0.290	−0.051	0.001	0.041
A. actinomycetemcomitans	-	0.075	0.167	0.060	0.193	0.077	0.040	−0.026	0.324*
P. gingivalis	0.075	-	0.565**	0.431**	0.549**	0.768**	0.077	−0.143	0.099
F. nucleatum	0.167	0.565**	-	0.662**	0.621**	0.766**	0.075	−0.054	0.274
P. micra	0.060	0.431**	0.662**	-	0.471**	0.673**	−0.115	0.098	0.257
P. intermedia	0.193	0.549**	0.621**	0.471**	-	0.641**	0.088	−0.080	0.202
C. rectus	0.077	0.768**	0.766**	0.673**	0.641**	-	0.065	−0.068	0.198
IL-1β (pg)	0.040	0.077	0.075	−0.115	0.088	0.065	-	−0.087	0.183
IL-17 (pg)	−0.026	−0.143	−0.054	0.098	−0.080	−0.068	−0.087	-	−0.168
GCF (μl)	0.324*	0.099	0.274	0.257	0.202	0.198	0.183	−0.168	-

Note: Correlation coefficient values by Spearman-correlation test. *$p < 0.05$, **$p < 0.01$.

Abbreviations: %, percentage; μl, microliter; *A. actinomycetemc*, *A. actinomycetemcomitans*; BOP, bleeding on probing; CAL, clinical attachment level; GCF, gingival crevicular fluid; GI, gingival index; IL, interleukin; mm, millimetre; PD, probing depth; pg, picogram; PI, plaque index.

TABLE 5 Comparison of counts (cells/ml × 10^3) of bacterial species among three treatment groups at baseline, 3 and 6 months

		GROUPS									
			(A)		(B)		(C)				
		Q-SRP	Q-SRP	FMD	FMD	FM-SRP	FM-SRP				
Test bacteria	Time points	No of positive patients	*N* = 14	No of positive patients	*N* = 14	No of positive patients	*N* = 14	(A-B-C) p^a	(A-B) p^b	(B-C) p^b	(A-C) p^b
A. actinomycetemcomitans	Baseline	**13**	14.2 (0.3–66.2)	**14**	4.4 (0.4–28.8)	**13**	0.9 (0.4–40.4)	0.898			
	3 months	**14**	1.3 (0.5–128.2)	**12**	0.8 (0.4–7.6)	**13**	0.9 (0.3–28.6)	0.490			
	6 months	**11**	0.6 (0.2–25.2)	**14**	0.5* (0.3–3.4)	**14**	1.1 (0.3–36.6)	0.530			
	p^c		0.607		**0.046**		0.880				
P. gingivalis	Baseline	**13**	432.7 (49.2–818.3)	**11**	8.2 (0.1–431.5)	**12**	499.3 (53.4–1086.7)	0.169			
	3 months	**11**	0.8*(0.2–30.6)	**8**	0.2 (0–0.9)	**10**	1.6* (0–11.1)	0.202			
	6 months	**11**	4.3*(0.1–71.7)	**8**	0.2 (0–2.1)	**8**	0.7* (0–11.8)	0.171			
	p^c		**0.002**		0.052		**<0.001**				
F. nucleatum	Baseline	**14**	62.1 (23.4–160.1)	**14**	79.7 (13.4–149.8)	**13**	42.1 (16.9–103)	0.692			
	3 months	**14**	20.5* (1.8–26.3)	**14**	9.2* (2.6–18)	**14**	26.8 (8.5–61.9)	0.069			
	6 months	**13**	9.6* (0.5–67.8)	**13**	8.4* (0.2–35.5)	**14**	9.6 (5.2–53.9)	0.523			
	p^c		**0.013**		**0.032**		0.145				
P. micra	Baseline	**14**	83.3 (27.3–157.9)	**14**	91.7 (39.6–287.9)	**14**	48.6 (17.9–125.8)	0.450			
	3 months	**14**	19.5 (11.7–51.3)	**14**	21.3*(11.9–30)	**14**	35.8 (10.1–81)	0.445			
	6 months	**14**	21.8 (6.4–49)	**14**	14.3*(7.3–90.7)	**14**	31.9 (11.1–79.3)	0.674			
	p^c		0.062		**0.002**		0.607				
P. intermedia	Baseline	**14**	293.8 (59.2–1742.7)	**13**	8.0 (1.2–135.9)	**14**	126.8 (37.9–269.1)	**0.005**	**0.003**	0.327	0.298
	3 months	**14**	4.5*(0.4–32)	**13**	0.3*(0.2–1.0)	**13**	1.1 (0.3–130.6)	**0.021**	**0.034**	0.074	1.000
	6 months	**11**	4.5* (0.3–80.5)	**12**	0.8 (0.1–4.3)	**13**	3.0 (0.3–9.1)	0.229			
	p^c		**0.005**		**0.032**		0.145				
C. rectus	Baseline	**14**	1549.1 (465.6–4277.8)	**14**	725.2 (301.9–3632.4)	**13**	1163.2 (193.8–4319.8)	0.630			
	3 months	**14**	47.5 (21.3–1180.1)	**14**	32.2*(14.2–201.4)	**14**	162.2 (39.3–1061.7)	0.192			
	6 months	**14**	115.0* (15.3–960.4)	**14**	25.5*(12.0–466.2)	**13**	179.7 (11.6–385.2)	0.674			
	p^c		**0.024**		**<0.001**		0.076				

TABLE 5 (Continued)

Test bacteria	Time points	GROUPS (A) Q-SRP No of positive patients	(A) Q-SRP N = 14	(B) FMD No of positive patients	(B) FMD N = 14	(C) FM-SRP No of positive patients	(C) FM-SRP N = 14	(A-B-C) p^a	(A-B) p^b	(B-C) p^b	(A-C) p^b
Total tested bacteria	Baseline		2501.7 (753.8–10307.6)		1109.7 (420.5–4746.4)		1995.3 (325.2–6121.8)	0.410			
	3 months		249.6* (111.4–1293)		75.1*(34.5–278.8)		393.2 (163.1–1465.3)	**0.041**	0.207	**0.045**	1.000
	6 months		279.6* (24.8–2138.6)		70.6*(27.9–667.9)		258.0 (53.8–659.4)	0.634			
	p^c		**0.013**		**0.005**		0.076				

Note: Data are presented as median (Q1–Q3) values. Statistically significant differences are marked with boldface text.

*Significant difference from baseline (Bonferroni-corrected Wilcoxon signed-rank test), $p < 0.05$.

Abbreviations: FMD, full-mouth disinfection; FM-SRP, full-mouth-based scaling and root planing; Q-SRP, quadrant-based scaling and root planing.

[a]Kruskal–Wallis test.

[b]Bonferroni-corrected Mann–Whitney *U*-test.

[c]Friedman test, $p < 0.05$.

members of normal oral microbiome. Therefore, they are difficult or impossible to eradicate,[16] as also shown by our results. But, their amount rather than mere detection in a complex ecosystem is likely of importance for the upcoming periodontal status.

The present statistical analyses mainly compared treatment group-based data. Although box plots visualized the data distribution of selected variables for treatment groups, they indicated it in quartiles and outliers. To envisage how results changed in individual patients after treatment, we presented the bacterial data in line charts for each treatment group, separately. It appeared that the present test species formed roughly two groups, one with wider dispersed post-treatment counts and the other one with more even groupings. Interestingly, the more widespread group contained *A. actinomycetemcomitans*, *P. gingivalis* and *P. intermedia* which, based on over 30 years of extensive research, have been included in the traditional periodontitis-associated species. Our present study design did not permit further analyses of the relationships between individual count patterns of test species and respective clinical status or attempts to predict treatment outcome.

One potential strength of the present study is the parallel comparison of clinical, biochemical and microbiological aspects of three different NSPT strategies in GAgP. Conversely, a limitation is the low number of patients, which is attributable to the relative rarity of GAgP and the strict inclusion criteria used, and lack of biochemical and microbiological analysis in respect of multi-rooted and single-rooted teeth separately within or among groups due to utilization of pooled samples. The promising results from this study should be confirmed in a larger study population, only feasible in multi-centre studies. Moreover, future studies evaluating treatment time, patient-reported outcome measures and oral health-related quality of life among different SRP protocols are required, in addition to clinical and microbiological/biochemical analyses.

5 | CONCLUSION

Clinical outcome was better after FMD than the standard Q-SRP protocol. Furthermore, only FMD led to reductions in subgingival levels of tested bacterial species and in GCF levels of IL-1β. The results encourage further investigation of FMD in the treatment of GAgP or stage-III, grade-C periodontitis.

6 | CLINICAL RELEVANCE

6.1 | Scientific rationale for the study

Non-surgical periodontal treatment is the first step in the treatment of all periodontitis patients. There are only few studies evaluating different scaling and root planing strategies on severe cases as aggressive or stage-III, grade-C periodontitis, and both cytokine and microbiological responses to these treatments have not yet been compared.

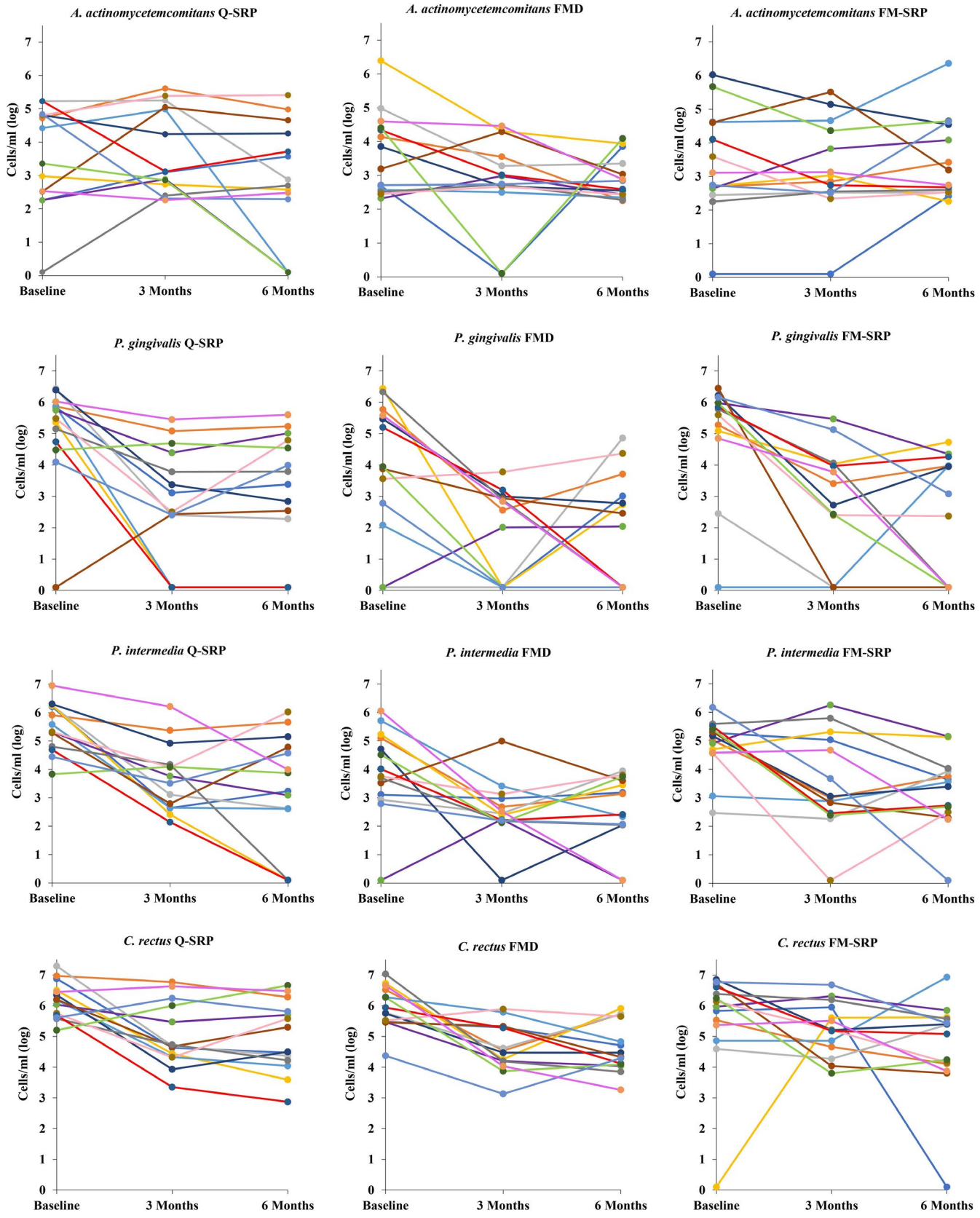

FIGURE 3 Line charts for changes in counts (log of cells/ml) of *A. actinomycetemcomitans*, *P. gingivalis*, *P. intermedia* and *C. rectus* for each patient allocated in different treatment groups at baseline, 3 and 6 months. Abbreviations: Q-SRP, quadrant-based scaling and root planing; FMD, full-mouth disinfection; FM-SRP, full-mouth scaling and root planing

6.2 | Principal findings

Full-mouth disinfection provided better clinical outcomes than the quadrant-based scaling and root planing. Furthermore, only full-mouth disinfection decreased the levels of IL-1β and five of six tested bacterial species.

6.3 | Practical implications

Full-mouth disinfection appears to provide a clinical advantage over quadrant-based scaling and root planing.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

Dilek Mamaklıoğlu involved in patient selection, sample collection, treatment procedures, data interpretation and manuscript writing. Maribasappa Karched involved in microbiological analysis and data interpretation. Leyla Kuru involved in randomization, biochemical analysis and critical reading. Bahar Kuru involved in manuscript writing and critical reading. Sirkka Asikainen involved in data interpretation, manuscript writing and critical writing. Başak Doğan involved in conception and design of the study, clinical measurement, data interpretation manuscript writing and critical reading. All authors have read and approved the final article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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