Received: 3 March 2017 | Revised: 6 September 2017 | Accepted: 24 September 2017

DOI: 10.1002/JPER.17-0148

JOURNAL OF Periodontology

HUMAN RANDOMIZED CONTROLLED TRIAL

The effect of twice daily kiwifruit consumption on periodontal and systemic conditions before and after treatment: A randomized clinical trial

Filippo Graziani[1,2,3] | Nicola Discepoli[2] | Stefano Gennai[1,2] | Dimitra Karapetsa[1,2] | Marco Nisi[2] | Lea Bianchi[4] | Nanning A. Martijn Rosema[5] | Ubele Van der Velden[5]

[1]Department of Surgical, Medical and Molecular Pathology and Critical Care Medicine, University of Pisa, Pisa, Italy

[2]Sub-Unit of Periodontology, Halitosis and Periodontal Medicine, University Hospital of Pisa, Pisa, Italy

[3]Interdepartmental Research Center "Nutraceuticals and Food for Health", University of Pisa, Pisa, Italy

[4]Chemistry and Endocrinology Laboratory, University Hospital of Pisa, Pisa, Italy

[5]Department of Periodontology, Academic Centre for Dentistry of Amsterdam (ACTA), University of Amsterdam and VU University of Amsterdam, The Netherlands

Correspondence
Prof. Filippo Graziani, Department of Surgical, Medical, Molecular and Critical Area Pathology, Unit of Dentistry and Oral Surgery, University Hospital of Pisa, Via Savi 10, 56126, Pisa, Italy.
Email: filippo.graziani@med.unipi.it

The first two authors equally contributed to the study

Abstract

Background: To assess the nutraceutical effects of twice/daily intake of kiwifruit on periodontal parameters and systemic health before and after initial periodontal treatment (IPT).

Methods: At baseline, participants were randomly assigned to test and control group, and either consumed two kiwifruits/day for 5 months or no kiwifruit. In the first 2 months, no periodontal treatment was delivered (2 M). Subsequently, a session of full-mouth IPT within 24 hours was performed. Participants were then re-assessed after 3 months (5 M). Blood samples, evaluating systemic biomarkers and vital signs, were also collected atbaseline, 2 M, and 5 M.

Results: Groups were balanced at baseline. At 2 M no within-groups differences could be detected for any parameter but the bleeding score, which decreased significantly in the kiwifruit group by 6.67% ± 11.90% ($P < 0.01$). Comparison of test and control group showed that 2 months of kiwifruit consumption resulted in significant lower values of bleeding, plaque, and attachment loss. After IPT both groups demonstrated substantial significant clinical benefits however the control group showed significant greater reductions of bleeding, plaque and attachment loss than the test group. Systemic biomarkers and vital signs did not show clinically relevant differences between test and control group.

Conclusions: Kiwifruit consumption reduces gingival inflammation despite the lack of any periodontal instrumentation or patient's behavioral changes. No adjunctive effect to periodontal treatment of dietary intake of kiwifruit was noted. (NCT NCT03084484)

KEYWORDS

Fruit, inflammation, periodontal diseases, randomized clinical trial, therapy

1 | INTRODUCTION

Periodontitis, a destructive inflammatory disease of the supporting tissues of the teeth, is caused by an imbalance between the host defense and environmental factors like bacteria, smoking, and poor nutrition.[1] Thus, treatment should not focus exclusively on plaque control and removal of bacteria but also on improving host resistance. The latter may be achieved by smoking abstention, stress reduction, and a healthy diet.

Interventional nutritional studies on humans are not well represented within periodontal literature. A diet rich in vitamins C and D, antioxidants and fiber, maintained for 4 weeks, is capable to reduce gingival inflammation despite unchanged plaque levels.[2] A diet supplemented with two grapefruits daily for 2 weeks increased the vitamin C levels and improved sulcus bleeding scores whereas no changes in probing pocket depth were noted.[3] In a peculiar experiment, subjects assuming dietary habits such as the ones of the stone age humans (whole grains cereals, herbs, honey, milk, fish, berries, and meat from domestic animals) showed reduction of the gingival inflammation.[4] Speculations on the positive effects of this dietary changes on gingival inflammation are mainly resting on the supplementation of vitamins, anti-oxidants and calcium.[5]

An important aliment and possible source of beneficial nutrients is kiwifruit. Kiwifruits are one of the highest dietary sources of vitamin C as green kiwifruit contains 93 mg of vitamin C/100 g fruit whereas e.g. oranges and grapefruits contain 53 and 33 mg/100 g fruit, respectively.[6] Plasma vitamin C levels are inversely related to the severity of periodontitis.[3,7–10] The results of a recent case control study also showed that periodontitis patients have lower plasma vitamin C levels than individuals without periodontal breakdown.[11] Moreover, 19% of periodontitis patients appeared to be depleted of vitamin C although the estimated dietary intake of vitamin C was comparable. Therefore, supplementation of vitamin C may be important. Furthermore, kiwifruits show high quantities of antioxidants such as lutein, an oxycarotenoid, and alpha-linolenic acid, an omega-3 fatty acid, making the positive contributions of vitamin C only moderate compared to the phenolic compounds.[12,13] On these premises the consumption of two or three kiwifruits daily have been applied in medical trials showing reduction of blood pressure,[14] platelet aggregation and triglycerides levels[15] and increase of high-density lipoprotein(HDL)-cholesterol levels.[16,17]

Therefore, the aim of the present study was 2-fold. The first objective was to investigate the effect of twice daily kiwifruit consumption as sole treatment modality in untreated periodontitis, and 2 months after followed by initial periodontal therapy supported by continued kiwifruit consumption. The second objective was to investigate the effect of twice daily kiwifruit consumption on periodontal and systemic parameters of these periodontitis patients 3 months after treatment.

2 | MATERIALS AND METHODS

2.1 | Experimental patient population

This study was a single-centered randomized, parallel design, clinical trial with a 5-month follow up that involved individuals affected by periodontitis. The protocol of the study received approval from the ethical committee of the University Hospital of Pisa (#3729/2012), it was registered post-hoc within a clinical trial database (NCT NCT03084484) and it was conducted according to the principles outlined in the Declaration of Helsinki on experimentation involving human subjects.

Eligible patients were identified from the population referred to the Sub-Unit of Periodontology, Halitosis and Periodontal Medicine of the University Hospital of Pisa (Italy) from February 2013 until June 2015. All patients gave written informed consent, full medical and dental histories were recorded, and oral examination was performed. Patients presenting with proximal attachment loss of ≥3 mm in ≥2 non-adjacent teeth,[18] probing depth (PD) ≥4 mm and bleeding on probing on at least 25% of their total sites, and documented radiographic bone loss were considered eligible to participate in this study. Individuals were excluded from the study if they were 1) aged < 18 years or > 70 years, 2) pregnant or lactating females, 3) females using contraceptive pharmacologic medications, 4) reported diagnosis of any systemic illnesses including cardiovascular, renal, and liver diseases, 5) in need of antibiotic treatment during initial periodontal treatment (IPT), 6) IPT in the previous 6 months, 7) allergic to latex, kiwifruit and fruits in general, 8) suffering of eating or digestive disease or food intolerances, and 9) smoking > 20 cigarettes per day.

2.2 | Study design

Prior to the start of the study, patients were informed in detail about the objectives of the investigation, and those willing to participate were requested to sign an informed consent form. Individuals who volunteered to participate were included in the study and invited to another clinical session in which a clinical examination was performed and blood collection was taken (baseline, Fig. 1). Allocation envelopes were then opened and participants in the test group were prescribed kiwifruit twice daily. They were instructed to eat two kiwifruits per day during the entire study period. Ingredients present in kiwifruit are mainly amino acids, heavy metal elements and ions, phenols, and antioxidants.[19] Among the latter, vitamin C is highly represented as its consumption through kiwifruit intake may vary among 60 mg to 160 mg per 100 mg of pure fruit flesh according to the type of kiwifruit, with an approximate daily intake of 100–200 vitamin C per day in this trial.[19] The kiwifruits had to be provided by the participants themselves. No recommendation on the type of kiwifruit, brand or origin was delivered. Kiwifruit was suggested to be taken as a whole and not mixed with sugar or other ingredients. No changes to their routinely dietary habits were suggested. Participants were also given diaries to take annotation of the actual daily kiwifruit intake throughout the

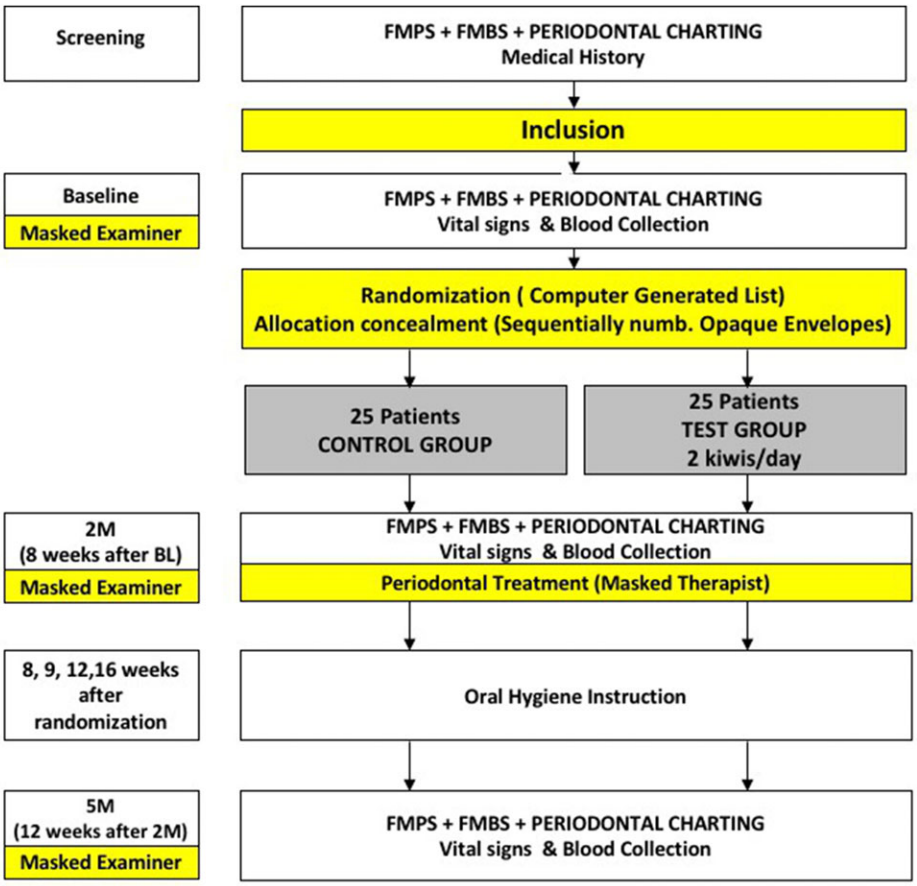

FIGURE 1 Study design

trial and eventual side-effects. In the control group, no dietary recommendations were given.

No treatment was delivered in the following 8 weeks which is the approximate usual waiting list period to receive treatment in our hospital in Pisa. During this period, no clinical sessions were performed unless an urgent appointment was requested. After 2 months (2 M) blood was again withdrawn and another clinical examination was performed. Subsequently, participants received full mouth IPT within 24 hours, consisting of root debridement, scaling and root planing in all sites showing PD $\geq$ 4 mm. Participants were also seen once a month to re-enforce oral hygiene. Three months after IPT (5 M) another clinical examination was performed and blood samples taken.

2.3 | Randomization procedures, allocation concealment, masking, and sample size calculation

Study participant numbers were assigned in ascending order at the enrollment visit. Participants were randomly assigned in a 1:1 ratio to either test or control group using a computer-generated table obtained by a random number generator. No stratification on cigarettes/day and years of smoking was made. The randomization table was saved by a research fellow not directly involved in the experimentation. Allocation to treatment was concealed to the clinical examiner (DK) and therapist (ND) with sealed opaque envelopes, which were opened by a clinical staff member on the day of the allocation, and were further concealed to statistician (UVDV). Patients were asked not to indicate their group allocation.

The sample size calculation was based on data of Staudte et al.[3] showing a reduction in bleeding scores from 1.68 $\pm$ 0.6 to 1.05 $\pm$ 0.6 mg/L after grapefruit consumption. Thus, 24 participants per treatment arm would be needed to provide 95% power to detect a difference of 0.6 between test and control group using the bleeding score after two months of kiwifruit consumption as the primary outcome variable, assuming that the standard deviation is 0.6. Thus, a sample of 50 participants, 25 per arm were recruited to compensate for possible drop-out.

2.4 | Clinical parameters

Both systemic and periodontal parameters were collected at baseline, 2 M, and 5 M.

Periodontal clinical parameters were assessed using a University of North Carolina 15-mm periodontal probe by the

clinical examiner at six sites/tooth, excluding third molars. Calibration of the examiner was performed on a total of 10 non-study patients affected by periodontitis. The examiner was judged to be reproducible after meeting a percentage of agreement of clinical attachment level (CAL) recording within ≤2 mm between two repeated measurements in separate occasions of at least 98%.[20] During the trial, full-mouth PD and recession of the gingival margin (REC), positive and negative, were recorded with measurements rounded off to the nearest millimeter. CAL was calculated as the sum of PD and REC. The full-mouth plaque score (FMPS) was measured as the percentage of the total surfaces showing plaque, assessed dichotomously on six surfaces per tooth.[21] Similarly, a full-mouth percentage bleeding score (FMBS) was calculated after assessing dichotomously the presence of bleeding on probing.[22]

During the study, blood samples were also collected and vital signs including systolic (SBP) and diastolic blood pressure (DBP) were measured in triplicates by using an automatic oscillometric device.* Average BP was then calculated from the last two measurements. Weight and height were measured and body mass index (BMI) was calculated. Body temperature was measured with tympanic reading by using an ear canal thermometer.† Smoking history was registered dichotomously as current or never/former.

2.5 | Blood collection and analysis of the serum markers

Serum samples were collected from a venipuncture in the antecubital fossa before 9.00 AM and after an overnight fast for all patients. Blood samples were immediately processed and serum aliquots were stored at −80°C. All laboratory analyses were performed at the laboratory of University Hospital of Pisa. Glycated hemoglobin (HbA1c), lipid fractions including total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides were measured using standard laboratory chemistry procedures. Serum C-reactive protein (CRP) was measured by immunoturbidometry.‡ To assess vitamin C, within 10 minutes after collection, sampling tubes were centrifuged with a low-speed centrifuge 3,500 rpm for 15 minutes§ to separate plasma from blood cells. Immediately thereafter, plasma was stabilized by means of a precipitation reagent to minimize the oxidation and subsequently prepared for vitamin C assessment by high-pressure liquid chromatography according to the manufacturer's instructions.¶

2.6 | Initial periodontal treatment

Supra- and sub-gingival mechanical instrumentation of the root surface (debridement, scaling and root planing), was performed by a single certified periodontist. Treatment was provided using both hand and ultrasonic instrumentation with periodontal tips.# Local anesthesia was used when needed and no time constraints were enforced. Participants received treatment within 24 hours in two separate sessions, one side of the mouth for each session.

Oral hygiene instruction consisting of electric tooth brushing and use of interdental brushes were carefully explained and demonstrated to the participants on the first day of periodontal treatment. Oral hygiene techniques were further reenforced after one week and once a month during follow-up.

2.7 | Statistical analysis

Descriptive statistics and data analyses were performed with statistical software.‖ All data are presented as mean and standard deviation unless otherwise specified. An intention-to-treat analysis, including the last observation carried forward technique, was performed.[23] Changes of oral and systemic parameters were analyzed in two fashions using mixed model analysis. Changes over time within test and control group were analyzed with analysis of variance (ANOVA) for repeated measures unadjusted for confounding factors, adopting least significant difference post hoc corrections. Differences in changes between test and control group over time were analyzed with a linear mixed model analysis including regimen variable, session variable and the interaction between regimen and session, adjusting for the outcome variable at baseline and the potential confounding factors such as age, sex, smoking status, BMI, vitamin C, and HbA1c.

3 | RESULTS

3.1 | Participant accountability, baseline characteristics, and dietary compliance

All recruited participants were Caucasians and all of them completed the study providing data for the final database analyses. Both groups were comparable for age, sex distribution, and smoking habits. Included individuals were on average at the beginning of their fifth decade of life, females accounted to 60% and 64%, and smokers 48% and 40% of the test and control groups, respectively. Among the two groups, participants did not differ in terms of systemic parameters and none of the included participants were undergoing hormone replacement treatment, anti-coagulant or anti-aggregation drugs. Overall,

* OMRON- 705IT, Omron, Kyoto, Japan

† Genius TM 2, Covidien, Dublin, Ireland

‡ Cobas, Roche Diagnostic, Mannheim, Germany

§ Heraeus Megafuge 40R, Thermo Fisher Scientific, Waltham, Massachusetts

¶ Eureka srl-Lab Division, Chiaravalle. Italy

EMS, Nyon, Switzerland

‖ SPSS, version 21.0, SPSS, Chicago, IL

TABLE 1 Demographic characteristics of the study sample

Variable mean ± SD or n (%)	Test Group (n = 25)	Control Group (n = 25)
Age, years	52.4 ± 9.2	50.4 ± 12.7
Sex, female (%)	15(60)	16(64)
Smoking, current (%)	12(48)	10(40)
Former smokers (%)	4 (16)	5(20)
BMI	23.9 ± 4.4	24.4 ± 3.6
Systolic BP, mmHg	125.0 ± 20.5	120.8 ± 18.7
Diastolic BP, mmHg	80.8 ± 10.5	76.0 ± 11.3
Total cholesterol, mmol/L	205.2 ± 35.3	216.6 ± 36.9
HDL, mmol/L	59.5 ± 15.7	61.1 ± 13.6
Triglycerides, mmol/L	94.6 ± 42.4	87.4 ± 34.2
CRP, mg/L	2.3 ± 2.8	1.5 ± 1.6
HbA1c, mmol/mol	38.9 ± 4.7	35.8 ± 3.6
Vitamin C, μmol/L	13.99 ± 19.26	16.61 ± 30.06
Number of teeth	26.2 ± 2.6	26.7 ± 2.7
FMBS, %	55.3 ± 17.8	62.8 ± 16.9
FMPS, %	74.8 ± 20.3	80.9 ± 11.8
CAL, mm	4.0 ± 0.6	4.2 ± 0.7

participants self-reported systemically healthy with a tendency for high-end levels of cholesterol, HbA1c, and CRP. Low levels of baseline vitamin C were noted. Differences were noted for baseline level of HbA1c indicating a lower glycemic metabolic control in the test group being at the threshold of prediabetes. Patients appeared to be affected by periodontal attachment loss higher than 4 mm on average, plaque score above 70% and inflammation observed in more than 50% of the sites analyzed (Table 1). No differences among the two groups were noted at baseline.

Daily kiwifruit intake was positively perceived by the study population as self-reported at 2 M and 5 M and adherence to dietary changes was high. The overall percentage of self-reported kiwifruit intake per day on the total of expected assumption (two kiwifruits per day over the course of 5 M) was from baseline to 2 M, 87.62% ± 14.63%, and from 2 M to 5 M, 78.37% ± 17.35% (difference baseline-2 M versus 2 M-5 M, P = 0.055). No major side effects were reported. One patient experienced 3 days of diarrhea, and one patient described 2 days of itching lips 9 days after the beginning of the consumption but kiwifruit intake was not discontinued.

3.2 | Periodontal parameters

In the first 2-month period, in which no treatment was performed, the control group did not show statistically significant changes of the periodontal parameters. In this group plaque levels remained above 80%, bleeding scores above 60%, and no changes of PD and CAL could be assessed (Table 2). Conversely, in the test group, FMBS decreased significantly by 6.67% ± 11.90% (P ≤ 0.01). The number of pockets also show a minor reduction in the test group (P < 0.05). Comparison of test and control groups showed significant differences for FMPS, FMBS, and CAL, in favor of the test group (Table 2). In the second period of the study, periodontal treatment appeared to be successful in both test and control groups. The only difference in this period was that treatment resulted in more reduction of FMBS, FMPS, and CAL in the control group (Table 2).

3.3 | Systemic biomarkers

In the first 2 months, no differences were noted among systemic biomarkers and vital signs in both groups compared to baseline (see supplementary Table 1 in online *Journal of Periodontology*). After 5 M, in the test group, vitamin C levels improved significantly compared to baseline (P < 0.05) from 13.99 ± 19.26 to 41.28 ± 37.07 μmol/L. Moreover, DBP decreased from 80.80 ± 10.48 to 77.00 ± 10.10 mmHg (P < 0.05). In the control group, no statistically significant changes could be assessed.

When comparing changes over time between test and controls, SBP showed a greater, yet modest, reduction in the first 2 months in the test group, −0.20 ± 13.81 versus 0.00 ± 12.99 mmHg (P = 0.034). After periodontal treatment an increased level of triglycerides (−15.88 ± 34.54 versus 1.40 ± 39.10 mmol/L, P ≤ 0.01) and a reduction of HDL (3.33 ± 14.51 versus −4.37 ± 7.41 mmol/L, P ≤ 0.05) were also noted in the test compared to the control group.

4 | DISCUSSION

This clinical trial compared the clinical effect of the consumption of two kiwifruits per day on both untreated and treated periodontal disease. This is the first trial evaluating this nutritional effect in such a model. The present data indicate that kiwifruit consumption establishes a modest, yet significant decrease of gingival inflammation and CAL gain in the absence of any treatment. Both phenomena possibly reflect a decrease of inflammation in periodontal tissues of the test group. The reduction of inflammation in the first 2 months may have also influenced plaque accumulation as, despite the absence of any treatment, FMPS increased in the control group and decreased in the test group. This might be due to the known effect of inflammation on plaque. Indeed, several studies have reported an increased plaque accumulation in the presence of gingival inflammation.[24–27] Also in experimental gingivitis studies it has been shown that individuals develop plaque more rapidly in the presence of gingivitis. [26,28,29]

The decrease in inflammation is in agreement with a previous observational study indicating reduction of gingival bleeding after 2 weeks of two grapefruit intake in patients with

TABLE 2 Clinical periodontal parameters of groups at various time points and differences between groups, presented as unadjusted data (ANOVA) and analyzed by linear mixed-model analysis (adjusted *P* values were corrected for baseline values of age, sex, smoking status, BMI, HbA1c, and vitamin C)

Variable (mean ± SD)	Time	Test group (n = 25)	Within test group difference	Control group (n = 25)	Within control group difference	Differences test vs control by time interaction	
						Unadjusted *P* value	Adjusted *P* value
FMBS, %	BL	55.30 ± 17.82		62.75 ± 16.94			
			6.67 ± 11.90[b]		−2.68 ± 8.23	<0.001	<0.001
	2 M	48.64 ± 18.64		65.21 ± 15.56			
			36.16 ± 20.39[c]		51.49 ± 15.99[c]	0.009	0.009
	5 M	12.48 ± 9.21[a]		13.72 ± 4.53[a]			
FMPS, %	BL	74.80 ± 20.26		80.87 ± 11.75			
			3.95 ± 12.95		−2.25 ± 11.1	0.009	0.001
	2 M	70.85 ± 20.55		83.52 ± 9.83			
			51.40 ± 20.92[c]		65.10 ± 13.97[c]	0.022	0.014
	5 M	19.45 ± 13.98[a]		18.42 ± 9.60[a]			
Recession, mm	BL	0.39 ± 0.48		0.37 ± 0.51			
			-0.03 ± 0.52		−0.02 ± 14.9	0.82	0.09
	2 M	0.42 ± 0.61		0.39 ± 0.48			
			−0.40 ± 0.62[c]		−0.46 ± 0.36[c]	0.97	0.19
	5 M	0.83 ± 0.65[a]		0.86 ± 0.54[a]			
Probing depth, mm	BL	3.79 ± 0.45		3.81 ± 0.53			
			0.04 ± 12.95		−0.01 ± 0.03	0.50	0.38
	2 M	3.74 ± 0.53		3.82 ± 0.47			
			1.14 ± 0.44[c]		1.29 ± 0.48[c]	0.22	0.15
	5 M	2.60 ± 0.34[a]		2.52 ± 0.31[a]			
Probing depth, ≥5 mm	BL	5.82 ± 0.39		5.73 ± 0.51			
			−0.03 ± 0.18		0.03 ± 0.15	0.44	0.42
	2 M	5.85 ± 0.48		5.70 ± 0.44			
			0.96 ± 1.18		0.46 ± 0.54	0.09	0.10
	5 M	4.97 ± 1.17		5.27 ± 0.28			
Number of pockets, ≥5 mm	BL	48.88 ± 17.29		54.32 ± 23.48			
			−0.03 ± 0.18		0.03 ± 0.15	0.08	0.06
	2 M	45.84 ± 21.62		53.64 ± 20.13			
			0.96 ± 1.18[c]		0.46 ± 0.54[c]	0.14	0.16
	5 M	6.36 ± 10.09[a]		6.08 ± 6.34[a]			
Clinical attachment level, mm	BL	4.02 ± 0.57		4.23 ± 0.67			
			0.03 ± 0.41		-0.06 ± 0.39	0.12	0.039
	2 M	3.99 ± 0.76		4.29 ± 0.81			
			0.66 ± 0.46[c]		0.89 ± 0.83[c]	0.16	0.031
	5 M	3.33 ± 0.71[a]		3.41 ± 0.61[a]			

[a]Significant difference compared to baseline P < 0.001

[b]Significant difference within test or control group $P \leq 0.01$

[c]Significant difference within test or control group $P < 0.001$

periodontitis.[3] In the present study this phenomenon might be due to the higher supplementation of antioxidants present in the kiwifruit such as vitamin C, omega-3 fatty acids and phenolic compounds. Vitamin C has a robust modulatory effect on gingival inflammation,[30] possibly diminishing inflammation through its reduction of the oxidative stress, downregulating inflammation, and improving endothelial function.[31,32] In the present study, after 5 M of kiwifruit consumption, the plasma vitamin C levels in the test group reached a level of about 40 μmol/L, which is in agreement with the literature.[33] In the first 2 months, however, the noted increase of vitamin C did not reach significance. A possible explanation may be the large variations in vitamin C levels in the participants. This could be related to the time of the day when kiwifruit was consumed, as the time of the day of consumption was not standardized in the present study. Indeed, the maximum plasma vitamin C level is reached 3 hours after kiwifruit consumption and steadily decreases thereafter.[34] Furthermore, this finding may be explained by the effect of other antioxidants such as the phenolic compounds.[12] Namely, a daily supplementation of 200 mg vitamin C together with 100 mg citrus flavonoids reduced both the subgingival load of all studied periodontal bacteria as well as the serum CRP levels, suggesting less inflammation, in an untreated periodontally diseased population deprived from regular dental care.[9] Kiwifruit is also rich in numerous antioxidants such as lutein, an oxycarotenoid, and alpha-linolenic acid, an omega-3 fatty acid.[13] Neutrophil chemotaxis and oxidant generation increased by 20% after kiwifruit supplementation,[35] while carotenoids and fatty acids both exhibit anti-inflammatory properties.[36]

No significant effect of kiwifruit consumption was noted as adjunctive to initial periodontal treatment. In fact, a higher FMBS and FMPS reduction and CAL gain in the control group was noted. These findings are probably due to the fact that in the test group some improvements of these parameters are already noted during the first 2 months of kiwifruit consumption. It is also likely that the magnitude of the effect of initial periodontal treatment is substantial to the extent that the possible benefit of kiwifruit consumption is overruled.

The systemic effects of the addition of daily kiwifruit to the diet was also analyzed as the medical literature has highlighted its effects on blood pressure and lipid metabolism[14,15] Interestingly, a significant reduction of diastolic blood pressure was noted in the kiwifruit group. This is in agreement with previous reports indicating significant reduction of both systolic and diastolic blood pressure modulated by kiwifruit consumption.[14,37] The mechanisms for such effects are hypothesized to rest in the increase of both potassium[38] and the vitamin C[39] intake provided by the kiwifruit.

Unexpectedly, no beneficial effects on lipid metabolism were seen, but a deterioration of the triglycerides in the kiwifruit group. This finding cannot be clearly explained. Kiwifruit consumption usually reduces the plasma values of triglycerides by approximately 15%.[15] However, although triglyceride values measured after 5 M of kiwifruit consumption were found significantly higher compared to those measured after 2Ms, at the start of the periodontal treatment, no difference was found in comparison to baseline values.

The authors are aware of the strength and the intrinsic limitations of the study. The sample size was calculated on the effect on the bleeding score. Thus, analysis on other parameters may be underpowered. Indeed, the results of the biomarkers should be cautiously interpreted as the sample size may not be sufficient to assess whether values are due to intrinsic fluctuations. Nevertheless, the present research model allows to measure the effect of the dietary consumption on both untreated and treated periodontal disease.

5 | CONCLUSIONS

Daily kiwifruit consumption determines a significant reduction of gingival inflammation in untreated periodontal disease. This may provide support for improved nutritional approaches in the prevention of periodontal diseases. No adjunctive effects of kiwifruit consumption to periodontal treatment were noted.

ACKNOWLEDGMENTS

The authors are deeply grateful to the clinical and administrative staff members of the Unit of Dentistry and Oral Surgery of the University Hospital of Pisa for the valuable support throughout the trial and to Drs. Camillo Giacomelli and Maria Rita Sessa for their help in managing blood samples.

The study was partly funded by the Italian Ministry Health (Rome, Italy) and the Tuscan Region (Florence, Italy) (Grant #GR-2009-1592229 “Periodontal disease as emergent systemic pathology: development of a new clinical unit for patient global health care”) and partly self-supported by the Unit of Dentistry and Oral Surgery of the Department of Surgical and Medical Pathology of the University of Pisa. Prof. Graziani has previously received a research grant from Straumann (Basel, Switzerland) unrelated to this particular research. The authors report no conflicts of interest in connection with this study.

REFERENCES

1. Pihlstrom BL, Michalowicz BS, Johnson NW. Periodontal diseases. *The Lancet*. 2005;366:1809–1820.
2. Woelber JP, Bremer K, Vach K, et al. An oral health optimized diet can reduce gingival and periodontal inflammation in humans – a randomized controlled pilot study. *BMC Oral Health*. 2016;17:1–8.

3. Staudte H, Sigusch BW, Glockmann E. Grapefruit consumption improves vitamin C status in periodontitis patients. *Br Dent J*. 2005;199:213–217.
4. Baumgartner S, Imfeld T, Schicht O, Rath C, Persson RE, Persson GR. The Impact of the Stone Age Diet on Gingival Conditions in the Absence of Oral Hygiene. *J Periodontol*. 2009;80:759–768.
5. Van der Velden U, Kuzmanova D, Chapple ILC. Micronutritional approaches to periodontal therapy. *J Clin Periodontol*. 2011;38:142–158.
6. US Department of Agriculture, Agricultural Research Service, Nutrient Data Laboratory. USDA, National Nutrient Database for Standard Reference. Release 28. 2016. Available at: https://ndb.nal.usda.gov/ndb/foods/show/2284?manu=&fgcd=&ds=
7. Amarasena N, Ogawa H, Yoshihara A, Hanada N, Miyazaki H. Serum vitamin C-periodontal relationship in community-dwelling elderly Japanese. *J Clin Periodontol*. 2005;32:93–97.
8. Panjamurthy K, Manoharan S, Ramachandran CR. Lipid peroxidation and antioxidant status in patients with periodontitis. *Cell Mol Biol Lett*. 2005;10:255–264.
9. Timmerman MF, Amaliya, Abbas F, et al. Java project on periodontal diseases: the relationship between vitamin C and the severity of periodontitis. *J Clin Periodontol*. 2007;34:299–304.
10. Chapple ILC, Matthews JB. The role of reactive oxygen and antioxidant species in periodontal tissue destruction. *Periodontol 2000*. 2007;43:160–232.
11. Kuzmanova D, Jansen IDC, Schoenmaker T, et al. Vitamin C in plasma and leucocytes in relation to periodontitis. *J Clin Periodontol*. 2012;39:905–912.
12. Gorinstein S, Haruenkit R, Poovarodom S, et al. The comparative characteristics of snake and kiwi fruits. *Food Chem Toxicol*. 2009 Aug;4:1884–1891.
13. Drummond L. The composition and nutritional value of kiwifruit. *Adv Food Nutr Res*. 2013;68:33–57.
14. Karlsen A, Svendsen M, Seljeflot I, et al. Kiwifruit decreases blood pressure and whole-blood platelet aggregation in male smokers. *J Hum Hypertens*. 2013;27:126–130.
15. Duttaroy AK, Jørgensen A. Effects of kiwi fruit consumption on platelet aggregation and plasma lipids in healthy human volunteers. *Platelets*. 2009;15:287–292.
16. Chang W-H, Liu J-F. Effects of kiwifruit consumption on serum lipid profiles and antioxidative status in hyperlipidemic subjects. *International Journal of Food Sciences and Nutrition*. 2009;60:709–716.
17. Gammon CS, Kruger R, Minihane AM, Conlon CA, Hurst von PR, Stonehouse W. Kiwifruit consumption favourably affects plasma lipids in a randomised controlled trial in hypercholesterolaemic men. *Br J Nutr*. 2013;109:2208–2218.
18. Tonetti MS, Claffey N. European Workshop in Periodontology group C. *J Clin Periodontol*. 2005;32(Suppl.6):210–213.
19. Ma T, Sun X, Zhao J, et al. Nutrient compositions and antioxidant capacity of kiwifruit (Actinidia) and their relationship with flesh color and commercial value. *Food Chemistry*. 2017;218:294–304.
20. Graziani F, Cei S, La Ferla F, Vano M, Gabriele M, Tonetti M. Effects of non-surgical periodontal therapy on the glomerular filtration rate of the kidney: an exploratory trial. *J Clin Periodontol*. 2010;37:638–643.
21. O'Leary TJ, Drake RB, Naylor JE. The plaque control record. *J Periodontol*. 1972;43:38–38.
22. Ainamo J, Bay I. Problems and proposals for recording gingivitis and plaque. *Int Dent J*. 1975;25:229–235.
23. Hollis S, Campbell F. What is meant by intention to treat analysis? Survey of published randomised controlled trials. *BMJ*. 1999;319:670–674.
24. Lang NP, Cumming BR, Löe H. Toothbrushing frequency as it relates to plaque development and gingival health. *J Periodontol*. 1973;44:396–405.
25. Goh CJ, Waite IM, Groves BJ, Cornick DE. The influence of gingival inflammation and pocketing on the rate of plaque formation during non-surgical periodontal treatment. *Br Dent J*. 1986;161:165–169.
26. Ramberg P, Lindhe J, Dahlen G, Volpe AR. The influence of gingival inflammation on de novo plaque formation. *J Clin Periodontol*. 1994;21:51–56.
27. Rowshani B, Timmerman MF, Van der Velden U. Plaque development in relation to the periodontal condition and bacterial load of the saliva. *J Clin Periodontol*. 2004;31:214–218.
28. Quirynen M, Dekeyser C, van Steenberghe D. The influence of gingival inflammation, tooth type, and timing on the rate of plaque formation. *J Periodontol*. 1991;62:219–222.
29. Daly CG, Highfield JE. Effect of localized experimental gingivitis on early supragingival plaque accumulation. *J Clin Periodontol*. 1996;23:160–164.
30. Leggott PJ, Robertson PB, Jacob RA, Zambon JJ, Walsh M, Armitage GC. Effects of ascorbic acid depletion and supplementation on periodontal health and subgingival microflora in humans. *J Dent Res*. 1991;70:1531–1536.
31. Ashor AW, Siervo M, Lara J, Oggioni C, Afshar S, Mathers JC. Effect of vitamin C and vitamin E supplementation on endothelial function: a systematic review and meta-analysis of randomised controlled trials. *Br J Nutr*. 2015;113:1182–1194.
32. Ellulu MS, Rahmat A, Ismail P, Khaza'ai H, Abed Y. Effect of vitamin C on inflammation and metabolic markers in hypertensive and/or diabetic obese adults: a randomized controlled trial. *Drug Des Devel Ther*. 2015:3405–3412.
33. Carr AC, Pullar JM, Moran S, Vissers MCM. Bioavailability of vitamin C from kiwifruit in non-smoking males: determination of 'healthy' and "optimal" intakes. *J Nutr Sci*. 2012;1:e14.
34. Collins BH, Horská A, Hotten PM, Riddoch C, Collins AR. Kiwifruit protects against oxidative DNA damage in human cells and in vitro. *Nutr Cancer*. 2001;39:148–153.
35. Bozonet SM, Carr AC, Pullar JM, Vissers MCM. Enhanced human neutrophil vitamin C status, chemotaxis and oxidant generation following dietary supplementation with vitamin C-rich SunGold kiwifruit. *Nutrients*. 2015;7:2574–2588.
36. Helmersson J, Arnlov J, Larsson A, Basu S. Low dietary intake of beta-carotene, alpha-tocopherol and ascorbic acid is associated with increased inflammatory and oxidative stress status in a Swedish cohort. *Br J Nutr*. 2009;101:1775–1782.

37. Svendsen M, Tonstad S, Heggen E, et al. The effect of kiwifruit consumption on blood pressure in subjects with moderately elevated blood pressure: a randomized, controlled study. *Blood Press*. 2014;24:48–54.

38. Aburto NJ, Hanson S, Gutierrez H, Hooper L, Elliott P, Cappuccio FP. Effect of increased potassium intake on cardiovascular risk factors and disease: systematic review and meta-analyses. *BMJ*. 2013;346:f1378.

39. Juraschek SP, Guallar E, Appel LJ, Miller ER. Effects of vitamin C supplementation on blood pressure: a meta-analysis of randomized controlled trials. *Am J Clin Nutr*. 2012;95:1079–1088.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

How to cite this article: Graziani F, Discepoli N, Gennai S et al. The effect of twice daily kiwifruit consumption on periodontal and systemic conditions before and after treatment: A randomized clinical trial. *J Periodontol*. 2018;89:285–293. https://doi.org/10.1002/JPER.17-0148