HSPI The Open Access Publisher

JCAD JOURNAL OF CLINICAL ADVANCES IN DENTISTRY
ISSN 2640-2858

Research Article

Use of *Lactobacillus reuteri* DSM 17938 in the treatment of Stage II-III Periodontitis: Longitudinal Study of 36 Patients

Alessandra Laforgia*, Daniela Di Venere, Saverio Capodiferro, Vanja Granberg, Giuseppe Barile and Massimo Corsalini

Department of Interdisciplinary Medicine, University of Bari Aldo Moro, 70100 Bari, Italy

Abstract

Periodontal diseases are a consequence of the host's inflammatory and immune mechanisms against dysbiotic bacterial plaque.

Given the role of probiotics in biofilm control and modulation of dysbiosis, this study assessed the efficacy of a specific strain of Lactobacillus Reuteri, DSM 17938, in the treatment of stage II and III periodontitis.

36 patients were randomly allocated into two groups: group A, the treated group; and Group B, the control group.

The treated group and the control group both underwent initial periodontal debridement. Patients received medications after undergoing periodontal debridement. Clinical parameters were assessed at baseline and at 21 days.

All parameters evaluated, Probing Depth (PD), Full Mouth Bleeding score (FMBS), and Full Mouth Plaque Score (FMPS) showed a reduction over time in both groups. The treated group showed a better reduction ($p = 0.05$) for PD.

As far as the depth of probing is concerned, the decrease observed between the control group and the group treated with probiotics is such as to be considered statistically significant and since the average of the values for the treated group is higher than that of the control group, the use of probiotics has an efficacy of medium statistical importance in the treatment of periodontal disease.

More Information

***Address for correspondence:** Alessandra Laforgia, Department of Interdisciplinary Medicine, University of Bari Aldo Moro, 70100 Bari, Italy, Email: alessandra.laforgia@uniba.it massimo.corsalini@uniba.it

Submitted: February 02, 2024
Approved: March 09, 2024
Published: March 11, 2024

How to cite this article: Laforgia A, Di Venere D, Capodiferro S, Granberg V, Barile G, et al. Use of *Lactobacillus reuteri* DSM 17938 in the treatment of Stage II-III Periodontitis: Longitudinal Study of 36 Patients. J Clin Adv Dent. 2024; 8: 001-008.

DOI: 10.29328/journal.jcad.1001039

Keywords: Periodontal disease; Probiotics; *Lactobacillus reuteri*; Inflammation; Periodontitis; Oral health

Check for updates

OPEN ACCESS

Introduction

Periodontal disease is defined as a group of inflammatory diseases with a multifactorial etiology, affecting the superficial and deep supporting tissue of the dental organ [1,2]. There are generally two forms of disease: gingivitis and periodontitis; The former is a reversible inflammation limited to superficial tissues, while the latter causes the irreversible destruction of the tooth's supporting tissues over time [3].

Periodontal disease is one of the most common chronic non-communicable diseases in the world and is still the leading cause of dental loss in the population [4,5].

According *to the Global Burden of Disease 2010 study,* the global prevalence of severe periodontitis, standardised by age, in the twenty years from 1990 to 2010 was 11.2%, making it the sixth most common disease in the world [6].

Periodontal diseases are the consequence of the host's inflammatory and immune defense processes against bacterial plaque [7]. Bacteria, while representing the necessary etiological factor, are not sufficient on their own to determine the onset of the disease [8]. Individual genetic profiles, systemic (diabetes mellitus), behavioural (smoking) and local risk factors influence the onset, progression, and severity of the disease [9-11]. The main cause of periodontal disease is microbial [12] and the microorganisms involved are those 52 normally present in bacterial plaque.

Dental plaque is a polymicrobial community embedded in a predominantly polysaccharide matrix that forms on the tooth surface. It constitutes a unique ecosystem in the body as bacteria, adhering to a hard and non-exfoliate surface, could organize themselves into a biofilm. For the development of the biofilm, the mechanism of co-aggregation is fundamental,

which makes it possible to colonize other microorganisms that would not be able to adhere directly to the enamel surface of the tooth. The onset and progression of periodontitis are attributable to an individual susceptibility on a genetic basis (single nucleotide polymorphisms. Periodontitis is said to develop in a severe form in genetically predisposed individuals [10]; genetic susceptibility is thought to be due to variations in nucleotide sequences, among the most studied are variations in genes encoding IL-1); Behavioural (Smoking. The reasons for the higher incidence of periodontal disease among smokers [13] are explained by the ecological alterations induced by smoking at the subgingival level, such as the increase in temperature and the reduction of the partial pressure of oxygen, selecting a periodontal pathogenic bacterial flora. Smoking also modulates the host's immune and inflammatory response to bacterial plaque. Finally, the increased destruction of tissues is related to a reduced reparative capacity and lower perfusion at the level of the vascular microcirculation due to nicotine-induced vasoconstriction) and systemic (Diabetes mellitus. The increased prevalence of periodontitis among diabetic subjects is now scientifically known [14], so much so that Harald Löe defined periodontitis as the sixth complication of diabetes [15]).

In addition, local conditions that favor the retention and consequent accumulation of bacterial plaque or its progression to the subgingival environment can be considered as a local factor predisposing to the onset of periodontal disease.

This could, in part, explain the site-specificity of the disease. Lastly, it should be remembered that the intake of some drugs such as cyclosporine A, diphenyldantoin, estrogen-progestogens, and calcium channel blockers can affect the individual's inflammatory and immune response to the action of bacterial plaque.

When, due to an excess of these bacteria and/or a decrease in the body's immune defenses, the normal balance that keeps the tissues healthy is altered, i.e. a condition called "dysbiosis"[16] is established, a state of tissue suffering of an inflammatory nature is high lighted, at first limited to the superficial structures but which later, if not treated adequately, tends to extend to the periodontal tissues in its entirety, giving rise to the most complicated picture of periodontitis.

From these premises, the objective to be pursued in the periodontal field is the control of bacterial plaque, the main cause of the disease, through causal mechanical therapy and the use of antiseptics and systemic and local antibiotics. Although mechanical therapy has proved to be effective in removing biofilm, numerous studies have shown that periodontal recolonization by oral pathogens resumes after a short time [17], in addition to the fact that the associated use of chemotherapy is not always effective or possible also by virtue of the increase in the incidence of the serious problem of antibiotic resistance.

Recent scientific and clinical studies have shown that the local application of "beneficial" bacteria seems to interfere with recolonization after clinical procedures or at least delay relapses. It is for this reason that in recent years the scientific community has been looking with great interest at a new and modern approach to the treatment of gingivitis and more generally of periodontal diseases: bacteriotherapy [18]. This therapy uses what the WHO itself defines as probiotics, i.e., those live and viable microorganisms that, administered in adequate quantities, can improve human health through interactions with the host.

On the one hand, probiotics can compete with periodontal pathogens and modulate dysbiosis conditions, thus decreasing the overall immunogenicity of the oral microbiota, and on the other hand, they can modulate immune/inflammatory pathways to decrease the destructive inflammation of periodontitis and create an immune homeostasis that can be preserved by the host for a long time [19].

The presence of probiotics, in adequate concentrations of 108 CFU/mL, medication has been shown to reduce the number of periodontal pathogens, including *Actinomyces spp., Bacteroides spp., S. intermedius,* and *C. albicans* [20].

The impact that probiotics of the *Lactobacillus species* have on inhibiting the growth of periodontal pathogenic bacteria in the oral cavity has also been demonstrated [21-23].

There is a direct relationship between periodontal inflammation and destruction and reduced lactobacilli levels [24]; bacteria such as *Lactobacillus fermentum* and *Lactobacillus gasseri* in the oral cavity of patients with chronic periodontitis are less represented than in healthy patients [23].

There are a growing number of studies that have dealt with the effects of the "typed probiotic" on oral health [25]. In recent times, the use of *L. reuteri* (DSM 17938) has shown an action that can positively influence the reduction of the pathogenic bacterial load and inflammation of the periodontium [26].

This strain produces reuterin, a natural broad-spectrum antibacterial that strongly inhibits the growth of numerous pathogens responsible for oral diseases [27].

Treatment with this probiotic for a period of at least 3 months has been shown to significantly improve the clinical outcomes (plaque index, bleeding index, etc.) obtained with normal professional dental hygiene procedures thanks to numerous scientific studies [26,28].

It should be noted that this probiotic has long been used in childhood gastroenteritis with the aim of counteracting the action of intestinal pathogens responsible for the acute process; Therefore, by analogy, if we consider that the gastro-enteric apparatus begins anatomically from the mouth, the hypothesis is supported that at the base of different diseases

sustained by infectious agents there is precisely an "dysbiosis", oral or intestinal [29].

The purpose of this study was to present preliminary data from the use of the probiotic Reuterin® drops in the treatment of periodontitis as an adjunctive therapy to scaling and radical planning (SRP).

Materials and methods

40 patients with stage II-III periodontal disease, aged between 30 and 85 years, were recruited at the Complex Operative Unit of Odontostomatology of the University of Bari Aldo Moro.

Each patient was initially subjected to medical and odontostomatological anamnesis, clinical examination, radiographic, and compilation of periodontal records. The data collected in this way made it possible to proceed with the assignment of the stage and biological grade of periodontal disease [30].

Subsequently, all patients received education and motivation in home oral hygiene, tartar ablation, and root planing.

To be eligible for inclusion in the study, patients had to meet the following inclusion criteria: age greater than 18 years and clinical diagnosis of stage II-III periodontal disease.

On the other hand, patients on antibiotic therapy, patients with autoimmune and/or oncological diseases, and patients on therapy with drugs that can alter periodontal tissues (phenytoin, cyclosporine, nifedipine) were excluded from the study.

Following the inclusion and exclusion criteria, of the 40 patients, 36 were eligible for the study.

Subjects who met the inclusion criteria (36 patients) were provided with oral information and informed consent regarding the study protocol. Informed consent was signed and obtained from all study participants.

The patients who were found to be suitable for the study underwent a first periodontal examination during which the anamnestic data were recorded, and the periodontal record was compiled.

A treatment plan common to all patients was developed which included tartar removal using ultrasound instruments, scaling and root planing sessions by means of curettes, and motivation for home oral hygiene.

Clinical parameters were assessed using a manual Williams periodontal probe. To standardize the procedures, the evaluations were always performed by the same operator. It was not recommended to use oral antimicrobial preparations (chlorhexidine) or antibiotics during the study period.

Physical examination and periodontal probing at "baseline" (time zero) assessed probing depth (PD) measured in mm at 6 sites for each tooth, plaque index (FMPS), and bleeding index (FMBS).

The FMPS was assessed with the following formula: (number of plaque sites/total number of sites probed x 100) The FMBS was assessed with the following formula: (number of bleeding sites/total number of sites probed x 100).

Participants were randomized by the study coordinator into two treatment groups: Group A (18 patients treated with causal therapy + Reuterin®) and Group B (18 patients treated with causal therapy alone).

No patients received any mechanical periodontal treatment during the study period (between T0 and T1).

Group A took 5 drops of Reuterin® 2 times a day for 21 days.

Reuterin® drops (Nóos, Rome) is a food supplement based on live lactic acid bacteria containing the patented strain® *L. reuteri* DSM 17938. 5 mL of product contains 1 x 10^8 CFU of *L. reuteri*.

Follow-up visits were scheduled 3 weeks after initial treatment during which patients underwent a follow-up visit and re-evaluation of the periodontal values to verify any improvement in the same.

The *PD*, considering the average of the values detected in the probable sites for each arch, the *FMPS,* and the *FMBS*, the object of this study, were evaluated and recorded at baseline (T0), after the causal therapy session, and after 21 days (T1). The clinical parameters of the 18 patients in group A are shown in Table 1.

The average age of the participants was 63.1 (51 – 81) years. Women accounted for 44.4% of the sample and men for 55.6%.

The clinical parameters of the 18 patients in group B are shown in Table 2.

The average age of the participants was 62.33 (31 – 70) years. Women accounted for 44.4% of the sample and men for 55.6%.

At the 21-day follow-up visit, the 18 patients in group A reported no adverse effects.

The type of adverse event investigated was gastrointestinal disorders (diarrhea), dysgeusia and/or metallic taste, headache, and nausea and/or vomiting.

Adherence to the experimental protocol was also documented. All 18 subjects in group A completed the course of taking the probiotic as directed.

Table 1: Clinical parameters of the 18 patients in Group A

Patient	Periodontal values	T0	T1
1	*PD upper*	5,1	3,2
	PD lower	3,2	2,8
	FMPS	79,5	32
	FMBS	23,9	10,2
2	*PD upper*	8,3	5,3
	PD lower	4,8	3,1
	FMPS	78,8	23,5
	FMBS	13,5	11,53
3	*PD upper*	4,3	2,9
	PD lower	4,3	1,9
	FMPS	76,7	22,4
	FMBS	33,6	6,9
4	*PD upper*	4,7	1,9
	PD lower	5,2	1,4
	FMPS	60	32
	FMBS	42	18
5	*PD upper*	5,1	2,9
	PD lower	4,9	2,4
	FMPS	70	34,6
	FMBS	53,3	23
6	*PD upper*	4,8	2,3
	PD lower	4,9	2,3
	FMPS	61,5	51
	FMBS	32,6	12
7	*PD upper*	4,9	2,6
	PD lower	4,7	2,8
	FMPS	31,5	12
	FMBS	39,6	9,8
8	*PD upper*	5,3	3
	PD lower	4,7	3
	FMPS	63	23,1
	FMBS	67,6	20,4
9	*PD upper*	4,2	2,6
	PD lower	4,5	3
	FMPS	64,7	28.4
	FMBS	58,6	15,5
10	*PD upper*	4,5	3
	PD lower	5	3,2
	FMPS	62	47
	FMBS	38,6	11,6
11	*PD upper*	4,6	4,5
	PD lower	4,5	4,2
	FMPS	88	54
	FMBS	25,4	19,1
12	*PD upper*	5,4	4,9
	PD lower	5,2	4,8
	FMPS	40	19,4
	FMBS	51	24,5
13	*PD upper*	4,4	4
	PD lower	5	4,5
	FMPS	46,6	19,2
	FMBS	22,7	9
14	*PD upper*	4,1	3,6
	PD lower	4,5	3,6
	FMPS	77,9	25
	FMBS	21,8	9,4
15	*PD upper*	4,3	3,7
	PD lower	4	3,5
	FMPS	48,5	12,1
	FMBS	16,7	9,2
16	*PD upper*	4,2	3,8
	PD lower	4,3	3,9
	FMPS	33	9,6
	FMBS	6	0
17	*PD upper*	4,2	3,7
	PD lower	4,4	3,8
	FMPS	36	10,3
	FMBS	10,3	9,8
18	*PD upper*	5,8	4,7
	PD lower	5,2	4,3
	FMPS	31,4	15,7
	FMBS	9,5	5,3

[1]Group A clinical parameters

Table 2: Clinical parameters of the 18 patients in Group B.

Patient	Periodontal values	T0	T1
1	*PD upper*	4,3	2,6
	PD lower	5,3	3,7
	FMPS	45,2	14,3
	FMBS	38,3	15
2	*PD upper*	3,6	4
	PD lower	4	2,3
	FMPS	37,5	40,6
	FMBS	9,4	9,4
3	*PD upper*	4,7	4,1
	PD lower	4,9	4,5
	FMPS	64,1	34,4
	FMBS	60,5	25
4	*PD upper*	5	3,3
	PD lower	5,2	3,2
	FMPS	45,2	9,5
	FMBS	19,8	0
5	*PD upper*	5,8	5
	PD lower	5,6	4,8
	FMPS	70,3	49,6
	FMBS	36	18,3
6	*PD upper*	4	3
	PD lower	4,3	3,6
	FMPS	96	30,2
	FMBS	65,6	15,6
7	*PD upper*	4,4	3
	PD lower	4,3	3,8
	FMPS	21,3	0
	FMBS	27,8	26
8	*PD upper*	4	3,8
	PD lower	4	3,7
	FMPS	50	9,7
	FMBS	4	0
9	*PD upper*	4,2	3,4
	PD lower	4,3	4,1
	FMPS	85	22
	FMBS	32,1	11,6
10	*PD upper*	5,6	5,2
	PD lower	5,4	4,8
	FMPS	73,1	32,7
	FMBS	83,7	45,2
11	*PD upper*	4,3	3,3 4
	PD lower	4	42,9
	FMPS	64	21,4
	FMBS	26,8	
12	*PD upper*	5,2	4
	PD lower	5,3	3,8
	FMPS	53,3	17,7
	FMBS	49,5	12,4
13	*PD upper*	4,3	4,2 4
	PD lower	4	29
	FMPS	45	11
	FMBS	14	
14	*PD upper*	5	4,4
	PD lower	5,1	4,8
	FMPS	48,4	21,3
	FMBS	27,4	12,1
15	*PD upper*	5,2	5
	PD lower	5,5	5,2
	FMPS	48	23,6
	FMBS	26,7	11,4
16	*PD upper*	6,1	4
	PD lower	6,	4,8
	FMPS	83,3	68,8
	FMBS	47,9	27,1
17	*PD upper*	5,5	4,2
	PD lower	5	3,7
	FMPS	29,5	9
	FMBS	12	0
18	*PD upper*	4,6	3,5
	PD lower	5	3,6
	FMPS	64,1	23,4
	FMBS	36,5	15,9

[2]Group B clinical parameters

Statistical analysis

The statistical treatment of the data had the aim of evaluating the possibility of rejecting or not the null hypothesis according to which the clinical parameters measured at T1 were identical in both groups (test and control).

The data obtained from the measurement of the four quantitative parameters (upper PD, lower PD, FMPS, FMBS) were treated with a two-tailed T-Test for samples of dissimilar variance. The data for each of the parameters were shown as the mean of all patients and their standard deviation (Table 3).

Outliers were evaluated through the construction of Boxplot charts; On the other hand, the normal distribution of the data was assessed by comparing the mean, median, and skewness of the sets.

The comparison of the four parameters of interest at baseline and at the detection time of 21 days was carried out, through the comparison of means with the T-Test method. In addition, Cohen's D factor was calculated for the case series in which the null hypothesis H0 was rejected, to evaluate the importance of the effect of the two different treatments.

The two-tailed significance level was set at 5%, the T-test was applied to samples of dissimilar variance (heteroscedastic T-test).

Comparison between the two times T0 and T1. Of the four parameters. Data are shown as mean ± standard deviation

Results

Upper Probing Depth (PD upper)

The mean probing depth above baseline for the test group was 4.9 ± 1 mm and 4.8 ± 0.7 mm for the control group.

After 21 days of treatment, the mean upper PD for the test group showed a statistically significant reduction (p - value = 0.05) compared to that observed in the control group, with a mean of 3.5 ± 0.9 for the test group.

The decrease, i.e., the difference in mean values between T0 and T1 between treated patients (T0 – T1 = 1.4 ± 0.9), is greater than that between untreated patients (0.9 ± 0.7).

A p - value of 0.05 or less indicates that the data obtained (in this case the difference between means) is statistically significant. On the other hand, the data that allows us to determine whether this difference, in addition to not being random, is also a datum of practical interest is Cohen's D. This value is given by the ratio between the mean decreases of the two groups and the weighted mean variance of each. In this case, with a value of 0.68 corresponding to an overlap of 67%, it can be said that the observed effect is of medium importance (Table 4).

Lower Probing Depth (PD lower)

The mean probing depth below baseline for the test group was 4.6 ± 0.5 mm and 4.8 ± 0.6 mm for the control group.

After 21 days of treatment, the mean lower PD for the test group showed a statistically significant reduction (p - value = 0.05) compared to that observed in the control group, with a mean of 3.2 ± 0.9.

The decrease among treated patients (T0 – T1 = 1.4 ± 1.1), is greater than that between untreated patients (0.8 ± 0.6).

As for the previous parameter, Cohen's D has a value of 0.68, which corresponds to an overlap of 67%, which leads us to say that the observed effect is of medium importance (Table 4).

Full Mouth Plaque Score (FMPS)

The mean FMPS (%) at baseline was 58.3 ± 18.6 for the test group and 56.8 ± 19.8 for the control group. At the follow-up visit, after the use of the probiotic, the mean FMPS was 26.2 ± 13.6 for the test group, showing a non-statistically significant reduction (p - value = 0.72) compared to the reduction in the value obtained with causal therapy alone. The decrease among treated patients (T 0-T1 = 32.1 ± 13.9) is like that of untreated patients (30.3 ± 16.6).

Full Mouth Bleeding Score (FMBS)

The mean FMBS (%) at baseline was 31.5 ± 18 for the test group and 34.3 ± 20.9 for the control group. At the follow-up visit, after the use of the probiotic, the mean FMBS was 12.5 ± 6.4 for the test group, showing a non-statistically significant reduction (p - value = 0.99) compared to the reduction in

Table 4: Cohen's D data.

Clinical parameters	Cohen's D
PD lower (*mm*)	0,68
PD upper (*mm*)	0,68

Table 3: Statistics

	Control group			Patients treated			p - value
Clinical parameters	T0	T1	T0-T1	T0	T1	T0-T1	T0 *vs.* T1
PD upper (mm)	4.8 ± 0.7	3.9 ± 0.7	0.9 ± 0.7	4.9 ± 1	3.5 ± 0.9	1.4 ± 0.9	0,05
PD lower (mm)	4.8 ± 0.6	4.0 ± 0.7	0.8 ± 0.6	4.6 ± 0.5	3.2 ± 0.9	1.4 ± 1.1	0,05
FMPS (%)	56.8 ± 19.8	26.6 ± 16.8	30.3 ± 16.6	58.3 ± 18.6	26.2 ± 13.6	32.1 ± 13.9	0,72
FMBS (%)	34.3 ± 20.9	15.4 ± 11.1	18.9 ± 14.1	31.5 ± 18	12.5 ± 6.4	19 ± 13.8	0,99

[3]Comparison between the two times T0 and T1. Of the four parameters. Data are shown as mean ± standard deviation.

the value obtained with causal therapy alone. The decrease among treated patients (T 0 -T1 = 19 ± 13.8) is almost equal to that of untreated patients (18.9 ± 14.1).

Discussion

The clinical efficacy of non-surgical treatment is widely documented in the literature [31]: about 65% of initially pathological pockets (PD > 4 mm with the presence of bleeding on probing) can return to physiological levels ("closed" pocket). These clinical improvements are associated with a specific change in the composition of the supragingival and subgingival biofilm [32,33]. Although the efficacy of "*No Surgical Periodontal Therapy*" has been demonstrated in reducing the pocket depth and improving the level of clinical attachment, it sometimes proves to be insufficient both for anatomical reasons (very deep pockets and furcations) and for microbiological reasons (recolonization of sites by periodontal pathogens is frequent) [34].

If non-surgical treatment is not able, on its own, to induce the ecological changes necessary to achieve and maintain the desired clinical improvements over time, the understanding of the etiopathogenetic mechanism of periodontitis allows us to identify the need for any additional therapies: pharmacological therapies (topical and/or systemic) aimed at containing the bacterial insult.

It is important to note that the systemic administration of antibiotics is not without complications both from an individual and public health point of view regarding the increase in bacterial resistance [35].

The need for additive therapeutic alternatives free from major adverse events such as those mentioned above has prompted the scientific community to investigate the efficacy of probiotics in the treatment of periodontal disease.

In line with the above, the aim of the present study was to verify whether the daily consumption of a supplement based on *L. reuteri* DSM 17938 could help to reduce the values of pocket depth, plaque, and bleeding of treated patients and to maintain the expected clinical improvements over time.

To improve the impact of probiotic drops, probiotic application was initiated immediately after a complete mouth disinfection procedure [36].

The statistical analysis showed that all four parameters considered (PD upp., PD low., FMPS, FMBS) decreased statistically significantly over time in both groups compared.

The comparison between the mean decreases of clinical parameters in the two groups (control and treated) is statistically significant only in the case of the clinical parameters PD upper and PD lower. If in these cases, in fact, applying the T-Test, a p - value of 0.05 was obtained, in the case of FMBS and FMPS, the p - value values were >0.05, therefore the comparison between the two groups for the latter two clinical parameters is not statistically significant.

Since there is no targeted microbiological analysis, it is not possible to assert that during treatment there was a probiotic modification of the microbial flora and a reduction of periodontal pathogens. Similarly, it was not possible to test the effect of *L. reuteri* DSM 17938 in counteracting the production and release of inflammatory mediators involved in plaque-related oral pathologies.

The best ways to administer probiotics and the dosages needed for different preventive or therapeutic purposes are still being studied. Limitations of the present study include the relatively small number of participants and the short-term study period.

The continuation of this study will be necessary to identify the microbiological qualitative variations resulting from the treatment, to expand the sample and the duration of the study, to verify the long-term effects of the use of probiotics, to be able to identify more clearly a preventive rationale in the use of the same.

Conclusion

The use of probiotics for the maintenance of oral health and for the treatment of periodontal disease is a novelty in the scientific field.

The results obtained from this study are in line with what has been expressed in several scientific studies [26,28,37-39].

We can therefore conclude that, in terms of PD upper and PD lower clinical parameters, the decrease observed between the control group and the group treated with probiotics is such as to be considered statistically significant and since the mean of the values for the treated group is higher than that of the control group, the use of probiotics has an efficacy of medium statistical importance in the treatment of periodontal disease.

This change could be related to an increase in patients' compliance and adherence to oral hygiene rules; The small sample size and the short duration of the study do not allow us to specifically attribute probiotic therapy as the reason for an improvement in patients' oral health, although it is observable. Consequently, also considering the ease of intake and the absence of adverse events highlighted in scientific literature, it can be concluded that probiotics could constitute an interesting and promising field of intervention in periodontal therapy, to be further investigated to confirm their adjuvant action in 'support the traditional therapy of periodontal diseases which is currently based on the mechanical removal of bacterial biofilm, performed professionally in the dental clinic and through home oral hygiene by the patient himself, and on the possible surgical correction of the deepest defects.

References

1. Lindhe J, Lang P. Clinical Periodontology and Implant Dentistry. Milano: Edi-Ermes. 2008.
2. Valletta G, Matarasso S, Bucci E. The Pathology and Clinic of Periodontal Disease. Padova: Piccin Nuova Libraria. 2005.
3. Kornman KS. Nature of periodontal diseases: assessment and diagnosis. J Periodontal Res. 1987 May;22(3):192-204. doi: 10.1111/j.1600-0765.1987.tb01566.x. PMID: 2955097.
4. Tonetti MS, Bottenberg P, Conrads G, Eickholz P, Heasman P, Huysmans MC, López R, Madianos P, Müller F, Needleman I, Nyvad B, Preshaw PM, Pretty I, Renvert S, Schwendicke F, Trombelli L, van der Putten GJ, Vanobbergen J, West N, Young A, Paris S. Dental caries and periodontal diseases in the ageing population: call to action to protect and enhance oral health and well-being as an essential component of healthy ageing - Consensus report of group 4 of the joint EFP/ORCA workshop on the boundaries between caries and periodontal diseases. J Clin Periodontol. 2017 Mar;44 Suppl 18:S135-S144. doi: 10.1111/jcpe.12681. PMID: 28266112.
5. Berezow AB, Darveau RP. Microbial shift and periodontitis. Periodontol 2000. 2011 Feb;55(1):36-47. doi: 10.1111/j.1600-0757.2010.00350.x. PMID: 21134227; PMCID: PMC3058494.
6. Kassebaum NJ, Bernabé E, Dahiya M, Bhandari B, Murray CJ, Marcenes W. Global burden of severe periodontitis in 1990-2010: a systematic review and meta-regression. J Dent Res. 2014 Nov;93(11):1045-53. doi: 10.1177/0022034514552491. Epub 2014 Sep 26. PMID: 25261053; PMCID: PMC4293771.
7. Sanz M, van Winkelhoff AJ; Working Group 1 of Seventh European Workshop on Periodontology. Periodontal infections: understanding the complexity--consensus of the Seventh European Workshop on Periodontology. J Clin Periodontol. 2011 Mar;38 Suppl 11:3-6. doi: 10.1111/j.1600-051X.2010.01681.x. PMID: 21323698.
8. Darveau RP. Periodontitis: a polymicrobial disruption of host homeostasis. Nat Rev Microbiol. 2010 Jul;8(7):481-90. doi: 10.1038/nrmicro2337. PMID: 20514045.
9. Leite FRM, Nascimento GG, Scheutz F, López R. Effect of Smoking on Periodontitis: A Systematic Review and Meta-regression. Am J Prev Med. 2018 Jun;54(6):831-841. doi: 10.1016/j.amepre.2018.02.014. Epub 2018 Apr 12. PMID: 29656920.
10. Kinane DF, Preshaw PM, Loos BG; Working Group 2 of Seventh European Workshop on Periodontology. Host-response: understanding the cellular and molecular mechanisms of host-microbial interactions--consensus of the Seventh European Workshop on Periodontology. J Clin Periodontol. 2011 Mar;38 Suppl 11:44-8. doi: 10.1111/j.1600-051X.2010.01682.x. PMID: 21323703.
11. Taylor JJ, Preshaw PM, Lalla E. A review of the evidence for pathogenic mechanisms that may link periodontitis and diabetes. J Clin Periodontol. 2013 Apr;40 Suppl 14:S113-34. doi: 10.1111/jcpe.12059. PMID: 23627323.
12. Kassebaum NJ, Bernabé E, Dahiya M, Bhandari B, Murray CJ, Marcenes W. Global burden of severe periodontitis in 1990-2010: a systematic review and meta-regression. J Dent Res. 2014 Nov;93(11):1045-53. doi: 10.1177/0022034514552491. Epub 2014 Sep 26. PMID: 25261053; PMCID: PMC4293771.
13. Johnson GK, Guthmiller JM. The impact of cigarette smoking on periodontal disease and treatment. Periodontol 2000. 2007;44:178-94. doi: 10.1111/j.1600-0757.2007.00212.x. PMID: 17474933.
14. Mealey BL, Ocampo GL. Diabetes mellitus and periodontal disease. Periodontol 2000. 2007;44:127-53. doi: 10.1111/j.1600-0757.2006.00193.x. PMID: 17474930.
15. Löe H. Periodontal disease. The sixth complication of diabetes mellitus. Diabetes Care. 1993 Jan;16(1):329-34. PMID: 8422804.
16. Bartold PM, Van Dyke TE. Periodontitis: a host-mediated disruption of microbial homeostasis. Unlearning learned concepts. Periodontol 2000. 2013 Jun;62(1):203-17. doi: 10.1111/j.1600-0757.2012.00450.x. PMID: 23574467; PMCID: PMC3692012.
17. Sbordone L, Ramaglia L, Gulletta E, Iacono V. Recolonization of the subgingival microflora after scaling and root planing in human periodontitis. J Periodontol. 1990 Sep;61(9):579-84. doi: 10.1902/jop.1990.61.9.579. PMID: 2213468.
18. Tonetti MS, Chapple IL; Working Group 3 of Seventh European Workshop on Periodontology. Biological approaches to the development of novel periodontal therapies--consensus of the Seventh European Workshop on Periodontology. J Clin Periodontol. 2011 Mar;38 Suppl 11:114-8. doi: 10.1111/j.1600-051X.2010.01675.x. PMID: 21323708.
19. Allaker RP, Stephen AS. Use of Probiotics and Oral Health. Curr Oral Health Rep. 2017;4(4):309-318. doi: 10.1007/s40496-017-0159-6. Epub 2017 Oct 19. PMID: 29201598; PMCID: PMC5688201.
20. Volozhin AI, Il'in VK, Maksimovskiĭ IuM, Sidorenko AB, Istranov LP, Tsarev VN, Istranova EV, Aboiants RK. Razrabotka i primenenie parodontal'noĭ poviazki iz kollagena i suspenzii kletok Lactobacillus casei 37 v kompleksnom lechenii vospalitel'nykh zabolevaniĭ parodonta (rezul'taty mikrobiologicheskikh issledovaniĭ) [Development and use of periodontal dressing of collagen and Lactobacillus casei 37 cell suspension in combined treatment of periodontal disease of inflammatory origin (a microbiological study)]. Stomatologiia (Mosk). 2004;83(6):6-8. Russian. PMID: 15602477.
21. Sookkhee S, Chulasiri M, Prachyabrued W. Lactic acid bacteria from healthy oral cavity of Thai volunteers: inhibition of oral pathogens. J Appl Microbiol. 2001 Feb;90(2):172-9. doi: 10.1046/j.1365-2672.2001.01229.x. PMID: 11168719.
22. Ishikawa H, Aiba Y, Nakanishi M, Oh-hashi Y, Koga Y. Suppression of Periodontal Pathogenic Bacteria in the Saliva of Humans by the Administration of Lactobacillus salivarius TI2711. Nihon Shishubyo Gakkai Kaishi J Jpn Soc Periodontol. 2003;45(1):105–12.
23. Kõll-Klais P, Mändar R, Leibur E, Marcotte H, Hammarström L, Mikelsaar M. Oral lactobacilli in chronic periodontitis and periodontal health: species composition and antimicrobial activity. Oral Microbiol Immunol. 2005 Dec;20(6):354-61. doi: 10.1111/j.1399-302X.2005.00239.x. PMID: 16238595.
24. Kõll-Klais P, Mändar R, Leibur E, Marcotte H, Hammarström L, Mikelsaar M. Oral lactobacilli in chronic periodontitis and periodontal health: species composition and antimicrobial activity. Oral Microbiol Immunol. 2005 Dec;20(6):354-61. doi: 10.1111/j.1399-302X.2005.00239.x. PMID: 16238595.
25. Arpita R, Swetha J, Babu M, Sudhir R. Recent Trends in Non-Surgical Periodontal Care for the General Dentist. A Review. Bangladesh. J Dent Res Educ. 30 August 2014;4(2):78–82.
26. Vivekananda MR, Vandana KL, Bhat KG. Effect of the probiotic Lactobacilli reuteri (Prodentis) in the management of periodontal disease: a preliminary randomized clinical trial. J Oral Microbiol. 2010 Nov 2;2. doi: 10.3402/jom.v2i0.5344. PMID: 21523225; PMCID: PMC3084569.
27. Jones SE, Versalovic J. Probiotic Lactobacillus reuteri biofilms produce antimicrobial and anti-inflammatory factors. BMC Microbiol. 2009 Feb 11;9:35. doi: 10.1186/1471-2180-9-35. PMID: 19210794; PMCID: PMC2653509.
28. Teughels W, Durukan A, Ozcelik O, Pauwels M, Quirynen M, Haytac MC. Clinical and microbiological effects of Lactobacillus reuteri probiotics in the treatment of chronic periodontitis: a randomized placebo-controlled study. J Clin Periodontol. 2013 Nov;40(11):1025-35. doi: 10.1111/jcpe.12155. Epub 2013 Sep 15. PMID: 24164569; PMCID: PMC3908359.
29. Spinler JK, Sontakke A, Hollister EB, Venable SF, Oh PL, Balderas MA, Saulnier DM, Mistretta TA, Devaraj S, Walter J, Versalovic J, Highlander SK. From prediction to function using evolutionary genomics: human-specific ecotypes of Lactobacillus reuteri have diverse probiotic functions. Genome Biol Evol. 2014 Jun 19;6(7):1772-89. doi: 10.1093/gbe/evu137. PMID: 24951561; PMCID: PMC4122935.

30. Tonetti MS, Greenwell H, Kornman KS. Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. J Periodontol. 2018 Jun;89 Suppl 1:S159-S172. doi: 10.1002/JPER.18-0006. Erratum in: J Periodontol. 2018 Dec;89(12):1475. PMID: 29926952.

31. Suvan J, Leira Y, Moreno Sancho FM, Graziani F, Derks J, Tomasi C. Subgingival instrumentation for treatment of periodontitis. A systematic review. J Clin Periodontol. 2020 Jul;47 Suppl 22:155-175. doi: 10.1111/jcpe.13245. PMID: 31889320.

32. Cugini MA, Haffajee AD, Smith C, Kent RL Jr, Socransky SS. The effect of scaling and root planing on the clinical and microbiological parameters of periodontal diseases: 12-month results. J Clin Periodontol. 2000 Jan;27(1):30-6. doi: 10.1034/j.1600-051x.2000.027001030.x. PMID: 10674959.

33. Teles RP, Haffajee AD, Socransky SS. Microbiological goals of periodontal therapy. Periodontol 2000. 2006;42:180-218. doi: 10.1111/j.1600-0757.2006.00192.x. PMID: 16930311.

34. Haffajee AD, Teles RP, Socransky SS. The effect of periodontal therapy on the composition of the subgingival microbiota. Periodontol 2000. 2006;42:219-58. doi: 10.1111/j.1600-0757.2006.00191.x. PMID: 16930312.

35. Elias C, Moja L, Mertz D, Loeb M, Forte G, Magrini N. Guideline recommendations and antimicrobial resistance: the need for a change. BMJ Open. 2017 Jul 26;7(7):e016264. doi: 10.1136/bmjopen-2017-016264. PMID: 28751488; PMCID: PMC5642659.

36. Teughels W, Loozen G, Quirynen M. Do probiotics offer opportunities to manipulate the periodontal oral microbiota? J Clin Periodontol. 2011 Mar;38 Suppl 11:159-77. doi: 10.1111/j.1600-051X.2010.01665.x. PMID: 21323712.

37. İnce G, Gürsoy H, İpçi ŞD, Cakar G, Emekli-Alturfan E, Yılmaz S. Clinical and Biochemical Evaluation of Lozenges Containing Lactobacillus reuteri as an Adjunct to Non-Surgical Periodontal Therapy in Chronic Periodontitis. J Periodontol. 2015 Jun;86(6):746-54. doi: 10.1902/jop.2015.140612. Epub 2015 Mar 5. PMID: 25741580.

38. Szkaradkiewicz AK, Stopa J, Karpiński TM. Effect of oral administration involving a probiotic strain of Lactobacillus reuteri on pro-inflammatory cytokine response in patients with chronic periodontitis. Arch Immunol Ther Exp (Warsz). 2014 Dec;62(6):495-500. doi: 10.1007/s00005-014-0277-y. Epub 2014 Feb 9. PMID: 24509697; PMCID: PMC4244533.

39. Vicario M, Santos A, Violant D, Nart J, Giner L. Clinical changes in periodontal subjects with the probiotic Lactobacillus reuteri Prodentis: a preliminary randomized clinical trial. Acta Odontol Scand. 2013 May-Jul;71(3-4):813-9. doi: 10.3109/00016357.2012.734404. Epub 2012 Nov 26. PMID: 23176716.