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Clinical Evaluation of Effects of Probiotic Lozenges As An Adjunct To Non-Surgical Periodontal Therapy In Chronic Periodontitis Treatment: A Randomized Clinical Trial

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Abstract

Introduction: Microbial plaque and host response to bacterial toxins are the critical factors for the development of chronic periodontitis. Non-surgical periodontal therapy, i.e., Scaling and Root planing (SRP) is the gold standard periodontal treatment protocol although recolonization with pathogenic species takes place over a shorter period of time. Probiotics are live microorganisms administered orally as an adjunctive to SRP to improve periodontal outcome.

Objective: The main purpose of this article was to evaluate the effect of probiotics lozenges containing Bifidobacterium longum, Lactobacillus reuteri and Lactobacillus rhamnosus used as an adjunctive to scaling and root planing (SRP) in patients with chronic periodontitis.

Materials and methods: 30 chronic periodontitis patients, aged between 35 to 58 years categorized into two groups. Group I treated by SRP and probiotic lozenges, twice daily for 30 days. Group II was treated by SRP alone. Plaque index (PI), Gingival index (GI), Pocket depth (PD), Clinical attachment level (CAL) measured at baseline (Day 0) and 30 days postoperatively.

Results: There were significant reduction in PI, GI, PD and gain in CAL in both the groups 30 days post operatively. ($p<0.005$). GI and PD were found much

lower in test group than in control group. ($p<0.001$) However, no statistically significant difference was seen in terms of CAL between both the groups ($p<0.096$).

Conclusion: Probiotics has a beneficial clinical effect as an adjunct to SRP in the treatment of chronic periodontitis.

Keywords: Chronic periodontitis, Probiotics, Non-surgical periodontal therapy, Scaling and Root planing, Probiotic lozenges, Lactobacillus reuteri, Reuterin

Introduction

Chronic periodontitis (CP) is "an inflammatory disease of the supporting tissues of the teeth caused by specific microorganisms or groups of specific microorganisms, resulting in progressive destruction of the periodontal ligament and alveolar bone with increased probing depth formation, recession, or both." [1] Microbial plaque and host response to bacterial toxins are the main aetiological factors for the development of chronic periodontitis.[2] The goal of the periodontal therapy is to arrest the inflammatory processes by eliminating calcified bacterial deposits and the bacterial biofilm [3] in order to ensure biologic compatibility between the diseased periodontal radicular surface and new connective tissue attachment. [4] Non-surgical periodontal therapy, i.e. scaling and root planing (SRP), using hand instruments and ultrasonic devices, is the gold standard periodontal treatment protocol. [5] Although inadequate access and treatment of anatomically challenging areas such as furcations, grooves and deep pockets and the complexity of the microbial population around the periodontium facilitate recolonization of pathogenic species over a shorter period of time which led to the use of other adjunct modalities for treating chronic periodontitis to achieve therapeutic stability. Probiotics are "live non-pathogenic microorganisms that, when administered in adequate amounts, confer a health benefit to the host." [6] The term "probiotics" was first coined by Gibson and Roberfroid in 1995, where they used Bifidobacterium and Lactobacillus to deliver health-promoting benefits. [7] Probiotics are thought to act through a variety of mechanisms including the exclusion and competition with potential pathogens for nutrients and epithelial cell adhesion, production of antimicrobial substances against periodontopathogens, local and systemic immunomodulation and, enhancement of the mucosal barrier function. [8] Health benefits have been shown with a specific strain of probiotics of the following species: Lactobacillus, Leuconostoc, Bacillus, Escherichia coli, Bifidobacterium, Saccharomyces, Enterococcus, Streptococcus and Pediococcus. [9] But, Lactobacillus sp. and Bifidobacterium sp., which are the most commonly used strains for oral health benefit. Among lactobacilli species, L. reuteri and L. rhamnosus have specifically gained attention due to their ability to play a role in the maintenance of a healthy microbiota because it prevents the overgrowth of other pathogenic microorganisms in the oral cavity [10] and represses inflammatory mediators such as tumour necrosis factor-alpha, interleukin-8 and interleukin-1 beta in saliva. Twetman S. et. al observed in a study that when probiotic intake was stopped, the percentage of sites that bleed upon probing increased again. [11] Alshareef A. et. al [12] and İnce G. et.al [13] in their studies showed significant improvement in periodontal parameters like Probing Pocket Depth (PPD), Bleeding on Probing (BOP), Plaque Index (PI), Gingival Index (GI) in L. reuteri containing probiotic lozenges group after compared with SRP alone. However, Hallstrom et al. [14] Iniesta et al. [15] have failed to demonstrate the effect of probiotics either clinically or microbiologically in their studies. These controversial results of the previous literatures made probiotics a more interesting treatment strategy as an adjunct to non-surgical periodontal therapy in patients

with chronic periodontitis to be probed on with thorough clinical research. The aim of this 30 days clinical trial, therefore, was to evaluate the clinical effects of probiotic lozenges containing Bifidobacterium longum, Lactobacillus reuteri, and Lactobacillus rhamnosus with SRP versus the effects of SRP alone in the treatment of patients with chronic periodontitis.

Materials And Methods

Patient Selection and Study Design

This randomized, controlled, clinical trial was conducted in the department of Periodontics and Implantology, Haldia Institute of Dental Sciences and Research, Haldia, Purba Medinipur, West Bengal. The study protocol was reviewed and approved by the Institutional Scientific and Ethical Committee Review Board. The study related procedures were explained to all the patients in their known languages before they sign the informed consent forms.

The study sample consisted of 30 patients (20 males and 10 females, aged between 35 to 58 years,) diagnosed with CP according to the criteria of the American Academy of Periodontology Workshop, 1999. [16] [FIG.-1A, 1B) Patients were selected according to the following inclusion criteria: i) Patient exhibiting the presence of chronic periodontitis at least in two teeth in two different quadrants in both arches with probing pocket depth ≥ 4mm ≤ 8mm, ii) Patients with bleeding on probing (BOP) and radiographic signs of alveolar bone loss. While i) Patients with systemic diseases, ii) Patients with less than 16 natural teeth and with partial dentures or fixed prosthodontic appliances or teeth with grade III mobility within the studied area, iii) Periodontal treatment done within the previous 12 months iv) Used antibiotics within the previous 6 months and use of anti-inflammatory drugs within the past 3 months, v) Pregnant and lactating mother and use of hormonal contraceptives, vi) Smokers, Alcoholics or Drug addicts were excluded from the study.

Randomization and Treatment Groups : Patients who were eligible for study participation were randomly assigned to one of the two treatment groups according to a computer-based randomization program (www.randomizer. org/Copyright ©1997–2011 by Geoffrey C. Urbaniak and Scott Plous).

Test group (Probiotic + SRP group) (N=15): Received SRP + Probiotic-containing lozenges. (Candyflora, Eskag Pharma, India)

Control group (SRP group) (N=15): Treated with scaling and root planing (SRP) only.

Periodontal Therapy : Full-mouth supra gingival scaling and root planing (SRP), using hand instruments and ultra-sonic scalers and sub gingival curettage, using area specific Gracey curettes under infiltration local anaesthesia was performed in a single appointment for each patient in all the groups.

Prescription of Probiotic Lozenges: The probiotic lozenges (Candyflora, Eskag Pharma, India) were given twice a day to the test group after SRP. Each probiotic lozenge contains five bifid bacteria including Bifidobacterium longum, Lactobacillus reuteri and Lactobacillus rhamnosus [FIG.-5A, 5B] and control group was left with scaling and root planing only.

Clinical evaluation: The clinical parameters recorded were, Plaque index (PI) (Silness and Loe,1964) [17] Gingival index (GI) (Loe and Silness,1963) [18] Probing depth (PD), measured from the gingival margin to the base of the periodontal pocket [FIG.—3A, 3B] and Clinical attachment level (CAL), measured from the cementoenamel junction (CEJ) to the base of the pocket. All measurements were made by a single examiner using Williams periodontal probe to the nearest millimetre.

These measurements were made at baseline [Day 0] and at 30 days postoperatively.

Post operative instructions.

➢ Brush twice daily with soft toothbrush and toothpaste.

➢ Follow Modified Bass brushing technique. (Patients were demonstrated and motivated).

➢ Use dental floss.

➢ Avoid vigorous brushing.

➢ Avoid any deleterious oral habit.

Statistical Analysis

The collected data were statistically analyzed using IBM SPSS Statistics for Windows, Version 26.0. (Armonk, NY: IBM Corp). The descriptive analysis (range, mean, and standard deviation [SD]) was included in the software. Graphs and box plots were constructed using the GraphPad Prism for Windows, Version 9.0 (GraphPad Software, La Jolla California USA). The comparison before and after treatment for the same group was made by a paired t-test, while the comparison between groups was made by the unpaired student's t- test. The P-value ≤ 0.05 was considered as the level of significance.

Results

The results of the current study showed that, there were statistically significant reductions in PI, GI in both the groups 30 days postoperatively. [FIG.-2A, 2B] (Table –1,2) (Bar Graph—1) However, there was a significant decrease in the GI in test group (SRP and probiotic lozenges group) after 30 days compared with SRP alone. (t=14, <0.001) (Table –3) (Bar Graph—2)

The mean values of PD were much lower in both the groups after 30 days from baseline (Day 0). [FIG.-4A, 4B] (Table—1,2) (Bar Graph—1) However, the mean value differences of PD in test group was more than in control group during the study period. (t= 9.6, P<0.001) (Table –3) (Bar Graph—2)

The mean gain in Clinical attachment level (CAL) were revealed in both the groups between baseline and 30 days post-operatively, which was also found to be statistically significant (P value <0.001). (Table –1,2) (Bar Graph—1) But, there was statistically insignificant evidence of gain in CAL was more in the test group when compared to the control group (t=4.6, <0.096). (Table –3) (Bar Graph—2)

Discussion

According to the World Health Organization [WHO] global oral health data bank, periodontal diseases are prevalent both in developed and developing countries and affect about 10.5 to 12% of global population. [19] Chronic periodontitis detrimentally accounts the tooth supporting structures resulting in bone loss and ultimately tooth loss which has a direct impact on systemic health, mental and socio-economic status. Thus, chronic periodontitis is a major threat to population.

Among the numerous etiologic factors responsible for chronic periodontitis, dental plaque has been proved to be the most detrimental in the initiation and progression of periodontal diseases. Dysbiosis in oral microbial community dynamics instigates some virulent keystone pathogen of this community like Porphyromonas gingivalis, Tannerella forsythia, and Treponema denticola to release lipopolysaccharides (LPS, bacterial endotoxins) which stimulates the host response and results in host immune dysregulation and increased representation of periodontal pathogens, that bi-directionally promote one another and together drive destruction of the tooth supporting structures, including the periodontal ligament (PDL) and alveolar bone.[20]

Nonsurgical periodontal therapy (NSPT) is the first recommended approach to the control of periodontal infections which is considered to be the "gold standard" to which other treatment methods are compared.[21]

as it reduces the quantity of bacterial plaque to a level (critical) that results in an equilibrium between the residual microbes and the host response. Because of the development resistance of antibiotic and recurrent recolonization of managed sites with pathogenic organisms, there was a need for a new therapy model that can be introduced to periodontal disease. [22]

Probiotics are multiple strains of useful bacteria that, when consumed adequately, provide many health benefits to the host by killing or inhibition of pathogenic bacterial growth, modification of host immunity by reduction of pro-inflammatory and elevation of anti-inflammatory cytokines, and alteration of cell proliferation and apoptosis. [23] In accordance with some clinical studies done by Bustamante M. et al. (2019) [24] and Morales A. et al., (2018) [25] which revealed the efficacy of probiotics as an adjunct to SRP, our current study aimed to evaluate the impact of probiotics as an adjunctive therapy to nonsurgical periodontal treatments on the clinical periodontal outcomes in the treatments of chronic periodontitis.

Haffajee et al. (1997) [26] and Cugini et al. (2000) [27] reported that scaling and root planing resulted in significant decreases in DNA probe counts of some specific sub-gingival microbes which resulted in subsequent significant clinical reduction in gingival redness, bleeding on probing. The present study showed highly significant reduction in PI, GI, PD and gain in CAL 30 days after SRP with or without probiotic lozenges in both groups in agreement with the findings of previous studies.

In accordance to the study done by Ince G. et al. (2015) [28]and Martin-Cabezas R et al. (2016) [29] our present study revealed a statistically significant decrease in GI and PD in test group than in control group from baseline (Day 0) to 30 days post-operatively (p value <0.001). These results sheds light on the efficacy of probiotic lozenges containing Bifidobacterium longum, Lactobacillus reuteri, and Lactobacillus rhamnosus in decreasing the gingival inflammation due to its anti-microbial activity against pathogenic bacteria thus promoting subsequent periodontal healing. L. reuteri is known to produce an antimicrobial substance reuterin, which inhibits a wide range of pathogenic bacteria. Also strains of L. reuteri have demonstrated an ability to block binding of pathogenic bacteria to host tissue and showed their action on a wide variety of cells to modulate the immune system. [30] These possible mechanisms of action of L. reuteri might be the basis of a direct or indirect effect of anti-plaque properties and anti-inflammatory actions. [31] However, comparison of mean differences of gain in CAL between two groups showed statistically insignificant result. This may be due a short evaluation time of the study.

Thus, the results of the current study were in favour of the potential benefits of conventional non-surgical periodontal therapy. But after considering the challenges observed with it, the use of probiotics, employed in this study, was demonstrated clinically effective to be used as an adjunct to scaling and root planing in the treatment of chronic periodontitis.

Conclusion

Within the limitations of the present study, it can be concluded that, conventional non-surgical periodontal therapy alone or in combination with probiotics used as an adjunct has potentiality in augmentation of periodontal health. However, a large dichotomy is present regarding the use of probiotics in periodontics which made it a more interesting treatment modality to be probed on. Hence, additional researches including large study population and long term follow up are warranted to establish the

effectiveness of probiotics as an adjunct to the non-surgical periodontal therapy.

Table: 1 Statistical comparisons of Clinical Periodontal Parameters for test group

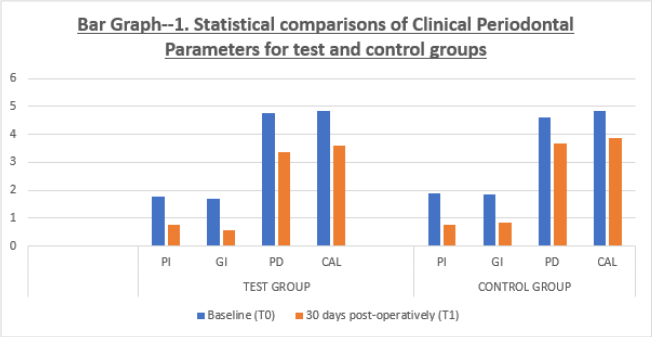
	Parameters	Time Intervals	Mean ± S.D	P-value
Test Group	PI	Baseline (T0)	1.77±0.127	0.005
		30 days post-operatively (T1)	0.747±0.117	
	GI	Baseline (T0)	1.7±0.294	0.005
		30 days post-operatively (T1)	0.577±0.0843	
	PD	Baseline (T0)	4.76±0.329	0.005
		30 days post-operatively (T1)	3.38±0.233	
	CAL	Baseline (T0)	4.84±0.223	0.005
		30 days post-operatively (T1)	3.58±0.305	

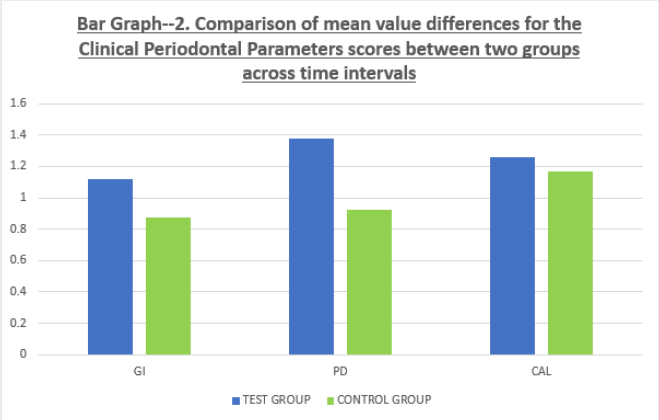
Table: 2 Statistical comparisons of Clinical Periodontal Parameters for control group

	Parameters	Time Intervals	Mean ± S.D	P-value
Control Group	PI	Baseline (T0)	1.87±0.171	0.003
		30 days post-operatively (T1)	0.77±0.145	
	GI	Baseline (T0)	1.85±0.246	0.005
		30 days post-operatively (T1)	0.823±0.0891	
	PD	Baseline (T0)	4.59±0.225	0.005
		30 days post-operatively (T1)	3.67±0.125	
	CAL	Baseline (T0)	4.86±0.209	0.003
		30 days post-operatively (T1)	3.86±0.0897	

Table 3: Comparison of mean value differences for the Clinical Periodontal Parameters scores between two groups across time intervals

Parameters	Test Group Differences of Mean ± S.D from baseline (T0) to 30 days (T1)	Control Group Differences of Mean ± S.D from baseline (T0) to 30 days (T1)	t-value	P-value
GI	1.12±0.302	0.875±0.267	14	<0.001
PD	1.38±0.299	0.924±0.247	9.6	<0.001
CAL	1.26±0.366	1.17±0.218	4.6	<0.096





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Legend Figures

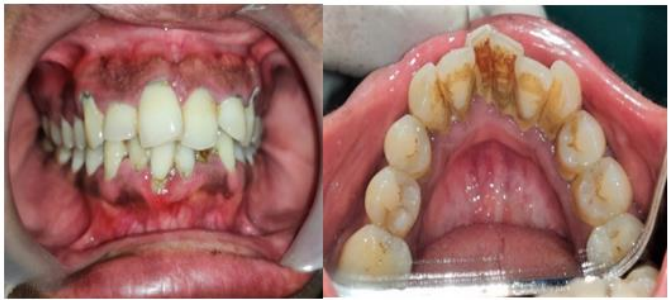

FIG.: 1A. PRE-OPERATIVE PHOTOGRAPHS
FIG.: 1B. PRE-OPERATIVE PHOTOGRAPHS
(LABIAL VIEW) (LINGUAL VIEW)

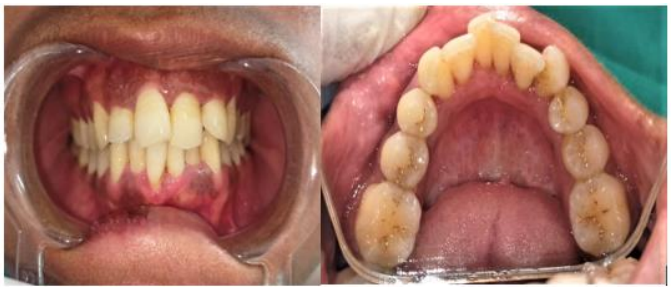

FIG.: 2A. PHOTOGRAPHS 30 DAYS POSTOPERATIVELY
FIG.: 2B. PHOTOGRAPHS 30 DAYS (LABIALVIEW) POST OPERATIVELY (LINGUAL VIEW)

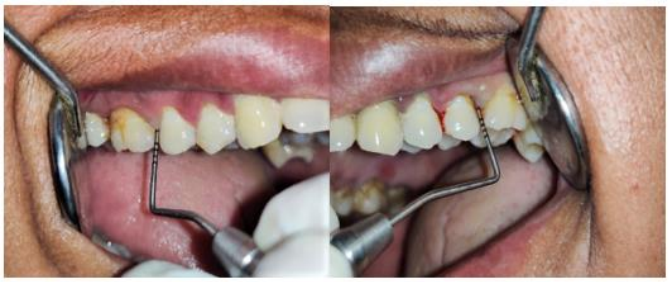

FIG.: 3A. PD AT BASELINE (TEST SIDE)
FIG.: 3B.PD AT BASELINE (CONTROL SIDE)

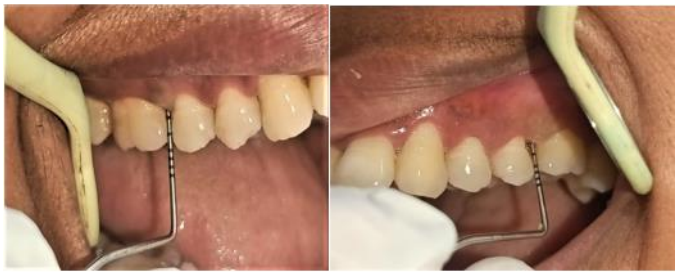

FIG.: 4A. PD AT 30 DAYS POSTOPERATIVELY
FIG.: 4B. PD AT 30 DAYS POSTOPERATIVELY
(TEST SIDE) (CONTROL SIDE)

FIG.: 5A. PROBIOTIC LOZENGES
FIG.: 5B. PROBIOTIC LOZENGES