

# Is Probiotic an Alternative to Systemic Antibiotics in treating Chronic Periodontitis?

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## ABSTRACT

**Aim:** to assess the clinical efficacy of three treatment modalities (*Lactobacillus reuteri* (*L. reuteri*) + Scaling and root planning (SRP), broad spectrum antibiotics+ SRP and SRP alone) and to compare their efficacy in the treatment of Chronic periodontitis.

**Methods:** Sixty systemically healthy participants (20 Group A, 20 Group B and 20 Group C), clinically diagnosed with CP were enrolled. All patients underwent SRP. Adjunctive Amoxicillin and metronidazole were given thrice and twice daily respectively for 7 days to the Group A participants. Adjunctive probiotic was given twice daily for 3 months to the Group B participants whereas, no adjunctive was provided to the participants of Group C.

**Results:** Statistically significant improvement was observed in the participants of each group A, B and C for every clinical parameter i.e., plaque index (PI), bleeding on probing (BOP), periodontal pocket depth (PPD) and clinical attachment level (CAL) gain on each follow-up visit. However, Group A and Group B exhibited superior results than Group C.

**Conclusion:** Treatment of CP with SRP along with adjunctive modalities improves clinical periodontal outcomes as compared to SRP alone. However, two adjunctive modalities i.e., systemic antibiotics and *L. reuteri* are comparable in efficacy.

**Keywords:** chronic periodontitis; probiotics; *Lactobacillus reuteri*; dental scaling; antibiotics

## INTRODUCTION

Microbial imbalance causing an increase in pathogenic bacteria and a decrease in beneficial bacteria in the susceptible individual are substantially the triggering factors for eliciting an inflammatory immune response. Inside the oral cavity such inflammatory response if remains persistent, leads to chronic periodontitis (CP)<sup>1</sup>. Gram-negative anaerobes *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola* are found to be associated with CP<sup>2</sup>. Dental plaque and calculus provide a suitable oxygen-free environment for the growth of these pathogenic microbes resulting in dysbiosis<sup>3,4</sup>.

Reduction in pathogenic bacterial load and disruption of plaque and calculus could not only prevents further damage but also resolves inflammation. Conventional non-surgical periodontal therapy includes scaling and root planing (SRP) which is considered to be the gold standard<sup>5</sup>. SRP mechanical debridement for the removal of soft and hard microbial deposits around the tooth at and below the gingival margins<sup>6</sup>. Although SRP is found to be effective in reducing pathogenic count but almost immediate

recolonization of microbial pathogens can impede healing<sup>7</sup>. Change in the local environment to prevent the recolonization of these pathogens and to improve clinical outcomes different therapeutic agents such as systemic antibiotics, laser and photodynamic therapy have been proposed as adjunctive along with SRP<sup>8,9</sup>. Among these adjunctive agents, systemic antibiotics are most commonly used and demonstrated promising results in improving periodontal outcomes<sup>2</sup>. These antibiotics have some infelicitous effects such as nausea, vomiting, diarrhea, antibacterial resistance, disruption of oral micro-flora, decrease in commensal microbes and increase in pathogenic microbes<sup>10,11</sup>. These effects limit their use and emphasize the need for an alternative treatment option with lesser or no side effect.

Since some "beneficial" bacteria or probiotics exhibit both antibacterial and anti-inflammatory properties<sup>12</sup>, their application as an alternate adjunctive can help to eliminate the deleterious effects inflicted by other treatment modalities. Several studies have shown improved clinical outcomes with the use of probiotics as an

adjunct<sup>13-15</sup>. Further studies are warranted to determine if probiotics have any effect on preventing and treating periodontal disease, as well as comparing their efficacy with other adjunctive therapies and SRP alone.

Therefore, our aim in this current study was to examine and compare the effectiveness of probiotics with SRP, systemic antibiotics with SRP, and SRP alone.

## MATERIAL AND METHODS

**Ethical guidelines:** The current study was conducted following the criteria acknowledged by the Declaration of Helsinki, as revised in 2013 for experimentation involving human subjects<sup>16</sup>. This randomized controlled clinical trial was double-blinded and designed to investigate the effectiveness of adjunctive probiotics to SRP in improving periodontal parameters in comparison to antibiotics + SRP & SRP alone. In order to conduct this study, approval was obtained from the Ethics Review Committee of Ziauddin University (reference code: 0220817SIOB) Karachi. Consolidated Standards of Reporting Trials (CONSORT) guidelines were followed and the Intervention was pre-registered in the database of [clinicaltrials.gov](http://clinicaltrials.gov) with reference number (identifier no. NCT03499184). All the participants were briefed about the complete study protocols before obtaining informed written consent.

**Patient selection criteria:** A total of 60 participants of both genders were selected after the screening of 117 patients from the outpatient department of Periodontology. 20 in each group A, B, and C aged  $\geq 30$  years, clinically diagnosed CP with periodontal pocket depth  $\geq 4$ mm were included in the study. The study participants had not taken part in any clinical trials over the period of the last two months and were in good health. No participant had ongoing antibiotic treatment or any systemic illness. Participants who were mentally handicapped, smokers, alcoholics, or who had undergone any periodontal therapy within the last 6 months. Pregnant and lactating women and those who failed to sign the consent form were excluded from the study. Patients with known systemic conditions (e.g. hormonal disorders, autoimmune disease, diabetes mellitus, osteoporosis, and immunological disorders) were also excluded as their condition could affect disease periodontal disease progression.

Received on 16-12-2022

Accepted on 26-05-2023

**Randomization:** Randomization using an opaque sealed envelope was used to allocate selected study participants into Group A (SRP + antibiotic), Group B (SRP + local probiotics), and Group C (SRP alone)(Fig.1). Randomization was conducted under the supervision of a research assistant. To ensure full blinding, random codes were generated for the study participants and were seized by the authorized research assistant till the end of data collection and analysis.

**Sample size calculation:** The sample size was determined using the clinical superiority trial formula, accounting for power 95% and the mean outcomes of the experimental and control groups. Each group was expected to contain 14 people, according to the calculations<sup>15</sup>. However, we have taken 20 participants in each of the three groups (Fig.1).

**Clinical assessment:** UNC probe 15 (Hu- Friedy, Chicago, IL) was used for the measurement of Clinical periodontal parameters, the results were recorded at baseline (day 0), 6 weeks, and 12 weeks(Fig.1). PI<sup>17</sup>, BOP<sup>18</sup>, PPD<sup>19</sup>, and CAL<sup>20</sup> were taken as primary outcomes and recorded from all the teeth except 3<sup>rd</sup> molars by a skilled investigator. PI and BOP were assessed based on the presence & absence from four sites and recorded. Whereas, 6 sites on individual teeth throughout the oral cavity were examined for the measurement of PPD and CAL.

After the baseline examination, all participants received oral hygiene instruction. The tooth brushing technique using the modified bass method was taught to participants and were advised to use the same non-medicated toothpaste twice daily throughout the study period. All the study participants had scaling and root planning performed by a skilled operator both manually (Hu-Friedy, Chicago, IL Gracey currettes) as well as through ultrasonic medical device (Guilin Zhuomuniao Medical Devices, China, Woodpecker; Ultrasonic Scaler).

Commercially available systemic antibiotics i.e., Amoxicillin 500mg and Metronidazole 400mg were provided to the respective study group (Group A). Probiotics in powdered form containing *lactobacillus reuteri* in concentration of 1.2 billion CFU/gm, packed in sachets were given to Group B. Participant of Group A were advised to take both antibiotics daily (Metronidazole in BD and Amoxicillin in TDS dosage) for the duration of 7 days. Whereas, Group B participants were instructed to mix the content of sachet with water and apply the resultant paste using toothbrush for 2 minutes after routine brushing & then rinse. Group C "Only SRP group" was not prescribed any post-interventional medication.

Patients were recalled after 6 weeks and 12 weeks and clinical parameters were measured and recorded on each visit. Whereas, saliva was collected at baseline and after 12 weeks.

**Data Analysis:** Statistical analysis of all the collected data was performed using Statistical Package for the Social Sciences (SPSS version. 23). Results were expressed in mean  $\pm$ SD and proportion as percentages. Intra-group comparisons were performed using repeated measured Analysis of Variance (ANOVA) and inter-group comparison at each interval was performed using ANOVA. A *P*-value less than 0.05 was taken as statistically significant.

## RESULTS

A total of 119 individuals were screened in the OPD of the Periodontology department and out of which 60 systemically healthy CP participants were recruited according to the defined eligibility criteria of CP. Thirty-four participants were males and 26 were females. The mean age was 40.4 $\pm$ 4.5, 41.3 $\pm$ 8.3, and 43.8 $\pm$ 4.9 years of the participants in groups A, B and C respectively (Table 1). No major side effects were observed. 3 patients from group A complained of gastric disturbance and bad taste. There were only 4 dropouts throughout the period of trial. Two from Group A, one from group B, and one from group C.

Baseline clinical periodontal parameters of all groups are shown (Table 2). Insignificant *P*-value shows that the baseline parameters of all the participants were comparable. Measurements of all parameters at baseline (day 0), 6 and 12-weeks intervals are given in (Table3). Intra-group analysis of each treatment group shows a significant decline in the values of all primary periodontal outcomes at 0-6 weeks, 6-12 weeks, and 0-12-week intervals (Table4). When the inter-group analysis was performed Group A & Group B showed comparable results for all the clinical parameters i.e., PPD, CAL, PI & BOP at each interval (Table 5). When Group B & Group C were compared and showed a substantial difference between the outcomes of the two groups. Group B demonstrate more PPD and BOP reduction and CAL gain as compared to Group C. However, the difference in PI between the two groups i.e., B & C was insignificant during 6-12-week intervals. When Group A was compared with Group C significant difference was observed between the two groups. Group A demonstrates a better reduction of PPD and BOP and more CAL gain. Whereas, for PI two groups showed significant difference during the first interval only i.e., 0-6-week interval.

Table 1: Demographic details of study participants.

Variables	Treatment Groups		
	Group A SRP+ Antibiotics	Group B SRP + Local Probiotics	Group C SRP alone
Number of patients (n)	20	20	20
Gender (Male/Female)	12/8	9/11	13/7
Age (mean in y $\pm$ SD)	40.4 $\pm$ 4.5	41.3 $\pm$ 8.3	43.8 $\pm$ 4.9

n; sample size, SD; standard deviation, SRP; scaling and root planing.

Table 2: Baseline measurement.

Variables	Treatment	Baseline	Difference in baseline values of all groups <i>P</i> -value
PPD (mm)	GROUP A	4.77 $\pm$ 0.61	.789
	GROUP B	4.86 $\pm$ 0.41	
	GROUP C	4.94 $\pm$ 1.18	
CAL (mm)	GROUP A	4.02 $\pm$ 0.615	.464
	GROUP B	3.97 $\pm$ 0.745	
	GROUP C	4.04 $\pm$ 0.74	
PI (%)	GROUP A	86.35 $\pm$ 9.82	.697
	GROUP B	86.20 $\pm$ 9.50	
	GROUP C	83.87 $\pm$ 8.97	
BOP (%)	GROUP A	72.09 $\pm$ 13.9	.940
	GROUP B	71.88 $\pm$ 11.14	
	GROUP C	73.24 $\pm$ 23.13	

Bold indicates statistical significance at *P* < 0.05, mm; millimeters, PPD; probing pocket depth, CAL; clinical attachment loss, PI; plaque index, BOP; bleeding on probing.

Table 3: Treatment outcome at three intervals.

Variables	Treatment	Baseline	6 Weeks	12 Weeks
PPD (mm)	GROUP A	4.77 ± 0.61	3.64 ± 0.55	2.88 ± 0.49
	GROUP B	4.86 ± 0.41	3.62 ± 0.52	2.91 ± 0.37
	GROUP C	4.94 ± 1.18	4.62 ± 0.93	4.34 ± 1.00
CAL (mm)	GROUP A	4.02 ± 0.615	3.65 ± 0.58	3.31 ± 0.57
	GROUP B	3.97 ± 0.745	3.60 ± 0.74	3.24 ± 0.80
	GROUP C	4.04 ± 0.74	3.88 ± 0.89	3.73 ± 0.59
PI (%)	GROUP A	86.35 ± 9.82	45.50 ± 8.57	28.17 ± 3.98
	GROUP B	86.20 ± 9.50	43.70 ± 8.95	19.10 ± 2.82
	GROUP C	83.87 ± 8.97	55.60 ± 8.13	32.51 ± 8.47
BOP (%)	GROUP A	72.09 ± 13.9	36.05 ± 7.02	14.8 ± 2.5
	GROUP B	71.88 ± 11.14	32.76 ± 6.86	13.42 ± 2.28
	GROUP C	73.24 ± 23.13	57.58 ± 12.77	44.83 ± 11.40

mm; millimeters, PPD; probing pocket depth, CAL; clinical attachment loss, PI; plaque index, BOP; bleeding on probing

Table 4: Intra group analysis.

Variables	Treatment	Interval I (0-6 weeks) P-value	Interval II (6-12 weeks) P-value	Interval III (0-12 weeks) P-value
PPD (mm)	GROUP A	.000	.000	.000
	GROUP B	.000	.000	.000
	GROUP C	.000	.000	.000
CAL (mm)	GROUP A	.000	.000	.000
	GROUP B	.000	.000	.000
	GROUP C	.000	.000	.000
PI (%)	GROUP A	.001	.000	.000
	GROUP B	.000	.000	.000
	GROUP C	.000	.000	.000
BOP (%)	GROUP A	.000	.000	.000
	GROUP B	.000	.000	.000
	GROUP C	.000	.000	.000

mm; millimeters, PPD; probing pocket depth, CAL; clinical attachment loss, PI; plaque index, BOP; bleeding on probing.

Table 5: Inter group analysis.

Variables	Treatment		Intervals		
			Baseline-6 weeks	6week-12 weeks	Baseline to 12 weeks
PPD (mm)	Group A	Group B	.132	.739	.755
	Group B	Group C	.000	.000	.000
	Group A	Group C	.000	.000	.000
CAL (mm)	Group A	Group B	.970	.920	.925
	Group B	Group C	.000	.001	.000
	Group A	Group C	.000	.002	.000
PI (%)	Group A	Group B	.758	.052	.037
	Group B	Group C	.000	.974	.000
	Group A	Group C	.000	.085	.141
BOP (%)	Group A	Group B	.293	.576	.920
	Group B	Group C	.000	.002	.000
	Group A	Group C	.000	.000	.000

mm; millimeters, PPD; probing pocket depth, CAL; clinical attachment loss, PI; plaque index, BOP; bleeding on probing.

## DISCUSSION

Mechanical debridement by SRP alone is still considered as a gold standard for CP and its effects in improving periodontal health are reported in literature<sup>21,22</sup>. Previous literature has compared the efficacy of SRP alone & SRP with systemic antibiotics<sup>22,23</sup>. To date, none of the published studies has compared the outcomes of adjunctive probiotics with SRP & adjunctive antibiotics with SRP and SRP alone. To the best of our knowledge, the current investigation is the first double-blinded, randomized controlled clinical trial designed to assess and evaluate the outcomes of three various modalities in CP patients. Current study demonstrated the resolution of inflammation and improvement in periodontal health in all three groups.

In this 12-week trial, CAL gain, PPD, BOP, and PI were taken as indicators of periodontal health & were analyzed at each interval. Results showed improvement in all primary periodontal parameters. Clinical indicators improved similarly in Groups A and B. But in Group C periodontal health improvement was considerably less.

In Group A, systemic antibiotics i.e., amoxicillin 500mg and metronidazole 400mg were given thrice and twice daily respectively, and showed significant improvement in all periodontal health indicators. Our results were similar to the previously

published studies<sup>24-26</sup>. Dina Zandbergen in her meta-analysis suggested this combination of antibiotics as efficacious and inexpensive supportive therapy for CP<sup>25</sup>. The keystone of periodontitis is sub-gingival pathogens which are continuously released in saliva. Saliva covering the whole of the oral cavity is responsible for pathogenic implantation. Therefore, the reduction of oral pathogen count by the administration of systemic antibiotics could be the cause of the improved clinical periodontal condition. In our study immersing all teeth<sup>26</sup>. Another study reported decreased levels of inflammatory cytokines in gingival crevices of the patients treated with amoxicillin & metronidazole adjunct to SRP<sup>27</sup> which could explain the resolution of inflammation in our study.

In group B, local probiotics *L.Reuteri* (DSM 17938) were used as an adjunct to SRP, and marked improvement in all the clinical periodontal outcomes was observed in the results. Our results are consistent with the previous studies<sup>1,15,28</sup>. Even Gizem Ince reported low levels of an inflammatory cytokine such as MMP-8 and high levels of TIMP (tissue inhibitors of matrix metalloproteinases) with the use of this probiotic<sup>28</sup>. Probiotics have several operating mechanisms to control infectious microorganisms either by providing "colonization resistance", "competitive exclusion", "immune regulation", or through their bactericidal action<sup>29</sup>. The exact mechanism which is responsible for oral tissue repair is still debatable. Maybe the combination of

their interaction with other microorganisms in dental plaque and their indirect influence on the immune system makes it possible to resolve inflammation & repair Periodontium<sup>30</sup>.

Although the results of Group C indicate some degree of improved periodontal health this improvement was far inferior to Group A and B suggested by the significant *P*-values when comparing Group A with Group C and Group B with group C (Table 5). Mechanical debridement of calcified deposits should be the first step to get rid of periodontal pathogens but this sole therapy is incapable of resolving inflammation. Poor instrumental access to deeper pockets & furcation areas provides hindrance to the removal of microbial deposits<sup>31</sup>. Also, immediate bacterial recolonization after SRP hampers the periodontal repair process<sup>7</sup>. Therefore, requires some additional therapy to control the microbial environment for better treatment outcomes. Intergroup comparison between Group A & Group B showed an insignificant difference for CAL gain, PPD, and BOP reduction in all intervals (Table 5) indicating that both adjunctives have similar efficacy. Only PI in 6-12 week intervals showed a significant difference in which greater reduction was observed in Group B which can be explained by the fact that effective brushing is the key to reduction in plaque accumulation<sup>32</sup>.

Taking into consideration the result of our study suggests a clear need for adjunctive along with SRP. Now with the fact that both systemic antibiotics and local probiotics have relatively similar efficacy against chronic periodontitis, it is difficult to recommend probiotics as an alternative to systemic antibiotics.

## CONCLUSION

SRP alone in the treatment of CP improved clinical outcomes of periodontal treatment. But addition of adjunctive therapies along with SRP can surely increase the possibility of superior outcomes in periodontal therapy. Choice of adjunctive is still debatable as based on clinical assessment both adjunctive in our study showed similar efficacy against CP.

**Conflict of interest:** The authors affirm no conflict of interest and all authors have studied and approved the final manuscript.

**Acknowledgement:** The authors would like to thank Board of Advanced Studies and Research, Ziauddin University, Karachi, Pakistan for funding this project.

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