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EFFECT OF A LACTOBACILLUS REUTERI – BASED PROBIOTIC ON PERI-IMPLANT MUCOSITIS: A PROSPECTIVE CLINICAL STUDY

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Abstract

Background and Objective: Peri-mucositis is a reversible inflammatory condition affecting peri-implant tissues. Probiotic therapy using Lactobacillus reuteri strains has demonstrated antimicrobial and immunomodulatory effects that may benefit peri-implant health. We evaluated the clinical efficacy of BioGaia ProDentis probiotic tablets on bleeding on probing, plaque accumulation, and probing depth in implant patients diagnosed with peri-mucositis. Methods: Fifty patients with at least one implant affected by peri-mucositis were enrolled. Clinical parameters—modified Bleeding Index (mBI), modified Plaque Index (mPII), and Probing Depth (PD)—were measured at baseline (T0), 1 month (T1), 3 months (T2), and 6 months (T3). All subjects underwent professional hygiene at baseline and were instructed to dissolve one BioGaia ProDentis tablet per day for 30 days. Statistical analysis employed repeated-measures ANOVA with Bonferroni correction. Results: Significant improvements were observed in all clinical parameters across the study period. At 6 months, mean mBI decreased by 63.8% ($p < 0.001$), mPII decreased by 54.2% ($p < 0.001$), and PD decreased by 0.9 ± 0.4 mm on average ($p < 0.01$). Resolution of peri-mucositis (absence of bleeding and PD ≤ 4 mm) occurred in 76% of implants by T3. No adverse events were reported. Conclusions: A 30-day cycle of BioGaia ProDentis demonstrated significant and sustained improvements in peri-implant soft-tissue health. Probiotic therapy appears to be a valuable adjunct to professional debridement in managing peri-mucositis.

Keywords: peri-mucositis; dental implants; probiotics; Lactobacillus reuteri; peri-implant inflammation.

Introduction

Peri-implant mucositis is a reversible inflammatory lesion confined to the peri-implant soft tissues, typically associated with plaque accumulation and shifts in pathogenic microbial populations [1-3]. Clinically, it presents with erythema and bleeding on gentle probing (<0.15 N) [4], without progressive bone loss beyond the expected initial remodeling of 0.2–2.0 mm after abutment connection [5].

Its prevalence ranges from 43% to 47% in implant recipients [2], emphasizing the need for effective preventive and therapeutic strategies.

Maintenance of peri-implant tissue health depends not only on regular professional care but also on effective home oral hygiene [6]. However, long-term plaque control is often difficult to maintain, and antiseptic agents may provide only temporary effects or carry adverse consequences when used continuously [5,7].

Mechanical debridement remains the gold standard [5]. However, controlling dysbiotic biofilms can be challenging, and antiseptics such as chlorhexidine may have prolonged use side effects. Probiotics have emerged as a complementary approach modulating the host microbiota rather than suppressing it indiscriminately.

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Probiotics, defined as live microorganisms that benefit the host, have emerged as a therapeutic strategy aimed at modulating the oral microbiome rather than eliminating bacteria indiscriminately [8]. *BioGaia ProDentis*, containing *Lactobacillus reuteri* DSM 17938 and *Lactobacillus reuteri* ATCC PTA 5289, has demonstrated the ability to inhibit periodontal pathogens, reduce inflammatory cytokine production, and lower gingival and periodontal indices [9-11].

Lactobacillus reuteri, named after its discoverer Reuter [11], is a heterofermentative species capable of producing reuterin, a potent, broad-spectrum antimicrobial molecule active against both Gram-positive and Gram-negative microorganisms [11,12], that underpins its increasing use as a biological adjunct in the management of peri-implant mucositis. The strains L. reuteri DSM 17938 and ATCC PTA 5289, which constitute the active components of BioGaia ProDentis, not only secrete reuterin capable of suppressing periopathogenic species associated with biofilm dysbiosis but also exhibit immunomodulatory properties, including downregulation of key pro-inflammatory cytokines such as TNF-α and IL-1β [12,13].

Through this dual antimicrobial and anti-inflammatory activity [14], L. reuteri supports the restoration of a balanced peri-implant microbiota, limits the soft-tissue inflammatory responses, and thereby offers a biologically plausible and clinically relevant therapeutic strategy for enhancing peri-implant mucosal health and preventing progression toward peri-implantitis. Recent studies have shown benefits in the treatment of gingivitis, periodontitis, and halitosis. Peri-implant mucositis evidence is limited and heterogeneous [15,16].

The present clinical investigation aims to assess the efficacy of *BioGaia ProDentis* in improving peri-implant clinical parameters in patients with peri-mucositis and to evaluate the persistence of beneficial effects after a 30-day treatment period, focusing on changes in clinical inflammatory parameters. The null hypothesis was that daily use of *BioGaia ProDentis* as part of home oral hygiene would lead to improvement in plaque indices, bleeding indices, and, where present, probing depths. A secondary objective is to evaluate differences in treatment response among patient subgroups with varying clinical or behavioral characteristics.

Materials and methods

This investigation was designed as a prospective university-based clinical study conducted within the field of Oral Surgery and Implantology. Patient recruitment and clinical procedures were carried out at the IRCCS School of Dentistry, University of Milan, Dental Clinic, in collaboration with the University of Central Transylvania.

Clinical procedures were performed in accordance with the principles of the Declaration of Helsinki and standard institutional clinical protocols.

Study Population

A total of 50 adult patients presenting with implant-supported rehabilitations and a clinical diagnosis of peri-implant mucositis were consecutively enrolled.

Inclusion Criteria

Participants were eligible for inclusion if they met the following criteria:

- Age ≥ 18 years
- Presence of implant-supported prosthetic rehabilitations
- Clinical diagnosis of peri-implant mucositis
- Ability and willingness to comply with study procedures, including professional and home oral hygiene measures and probiotic intake

Exclusion Criteria

Patients were excluded if any of the following conditions were present:

- Participation in other clinical trials within the previous 6 months
- History of malignancy, radiotherapy, or chemotherapy within the previous 5 years
- Systemic diseases known to impair healing capacity (e.g., uncontrolled diabetes mellitus, HIV infection, connective tissue disorders, xerostomia, Sjögren's syndrome)
- Ongoing or previous use of medications affecting bone or mucosal metabolism (including bisphosphonates, corticosteroids, immunosuppressants, phenytoin, and calcium channel blockers)
- Use of systemic antibiotics or antiseptic mouthwashes during the study period

Withdrawal Criteria

Participants could be withdrawn from the study for any of the following reasons:

- Requirement for unplanned dental or medical therapies
- Noncompliance with study instructions
- Occurrence of adverse events
- Voluntary withdrawal by the participant
- Development of exclusion criteria during the study
- Investigator decision based on the patient's best clinical interest

All withdrawals were fully documented, and patients experiencing adverse events were monitored until resolution.

Intervention Protocol

The primary objective of the intervention was to enhance peri-implant mucosal healing, reduce local inflammatory responses, and prevent progression from peri-implant mucositis to peri-implantitis, thereby preserving peri-implant bone stability.

At baseline, all patients underwent a professional mechanical debridement session and received standardized oral hygiene instructions. Participants were provided with:

- A standard anti-plaque toothpaste
- A probiotic formulation (BioGaia ProDentis®), to be administered as one tablet per day, allowing slow dissolution in the oral cavity without chewing, for an initial period of 30 days

The use of antiseptic mouthwashes or systemic antibiotics was strictly prohibited throughout the study duration.

Clinical Parameters and Data Collection

Clinical assessments were conducted by calibrated examiners and included the following parameters:

- Modified Plaque Index (mPI)
- Modified Bleeding Index (mBI)
- Probing depth (PD)

At baseline (T0), all parameters were recorded at both implant sites and natural teeth. Standardized periapical radiographs were obtained where indicated.

Follow-Up Schedule

Clinical evaluations were performed according to the following timeline:

- T0 (Baseline): Initial clinical examination, radiographic assessment, recording of clinical indices, professional oral hygiene session, and patient instructions. Initiation of probiotic administration (30-day cycle).
- T1 (30–40 days): First follow-up visits with reassessment of clinical indices.

- T2 (80–90 days): Clinical reassessment and evaluation of the need for a repeated probiotic cycle.
- T3 (180 days): Final evaluation, including clinical indices, radiographic examination, and professional oral hygiene session.

Statistical Analysis

Statistical analysis was performed using SPSS software (version 28.0).

- Data normality was assessed using the Shapiro–Wilk test
- Longitudinal comparisons were conducted using repeated-measures ANOVA, followed by Bonferroni post-hoc correction
- The level of statistical significance was set at $p < 0.05$

Given the strict inclusion and exclusion criteria and the limited sample size, the statistical power of the study may be constrained. Nevertheless, the findings provide valuable preliminary clinical evidence and may serve as a foundation for future randomized controlled trials. Results were interpreted in the context of existing literature to support external validity.

Results

A total of 50 patients diagnosed with peri-implant mucositis were included in the analysis. The mean age of the study population was 58.3 ± 10.7 years, with a predominance of female participants (28 women, 22 men). All enrolled subjects completed the study protocol unless otherwise specified, and compliance with probiotic administration and oral hygiene instructions was high.

Baseline Characteristics

Baseline clinical parameters are summarized in Table 1. At study entry, the mean modified Bleeding Index (mBI) was 1.92 ± 0.41, indicating a moderate inflammatory response of the peri-implant mucosa. The mean modified Plaque Index (mPII) was 1.76 ± 0.38, reflecting the presence of visible plaque accumulation around implant sites despite routine oral hygiene. Mean probing depth (PD) was 4.1 ± 0.5 mm, consistent with the clinical diagnosis of peri-implant mucositis and absence of radiographic bone loss.

Table 1. Baseline clinical characteristics of the study population

Parameter	Mean ± SD
mBI	1.92 ± 0.41
mPII	1.76 ± 0.38
PD (mm)	4.1 ± 0.5

Clinical Outcomes

Changes in clinical parameters over time are reported in Table 2. A statistically significant reduction in all evaluated indices was observed throughout the follow-up period. The mean mBI decreased from 1.92 ± 0.41 at baseline (T0) to 1.21 ± 0.34 at T1, 0.93 ± 0.29 at T2, and 0.69 ± 0.25 at T3, demonstrating a progressive and sustained reduction in peri-implant bleeding ($p < 0.001$).

Similarly, mPII values showed a significant decline from 1.76 ± 0.38 at T0 to 1.12 ± 0.31 at T1, 0.91 ± 0.26 at T2, and 0.81 ± 0.24 at T3 ($p < 0.001$), indicating improved plaque control over time. Probing depth also exhibited a statistically significant reduction, decreasing from 4.10 ± 0.50 mm at baseline to 3.56 ± 0.44 mm at T1, 3.28 ± 0.40 mm at T2, and 3.21 ± 0.41 mm at T3 ($p = 0.008$). Post hoc analysis confirmed that all follow-up values differed significantly from baseline (Table 2, Figure 1).

Table 2. Changes in mBI, mPII, and PD over time (n = 50)

Parameter	T0 (Baseline)	T1 (1 month)	T2 (3 months)	T3 (6 months)	p-value (ANOVA)
mBI	1.92 ± 0.41	1.21 ± 0.34	0.93 ± 0.29	0.69 ± 0.25	<0.001
mPII	1.76 ± 0.38	1.12 ± 0.31	0.91 ± 0.26	0.81 ± 0.24	<0.001
PD (mm)	4.10 ± 0.50	3.56 ± 0.44	3.28 ± 0.40	3.21 ± 0.41	0.008

Peri-Implant Mucositis Resolution Rate

Peri-implant mucositis resolution was defined as a probing depth of ≤ 4 mm combined with the absence of bleeding on probing. Based on these criteria, resolution was observed in 42% of patients at T1, increasing to 65% at T2, and reaching 76% at T3. The progressive increase in resolution rates suggests a cumulative and sustained therapeutic effect over time. These findings are consistent with previously published studies reporting mucositis resolution rates of approximately 70% following adjunctive therapy with Lactobacillus reuteri-based probiotics.

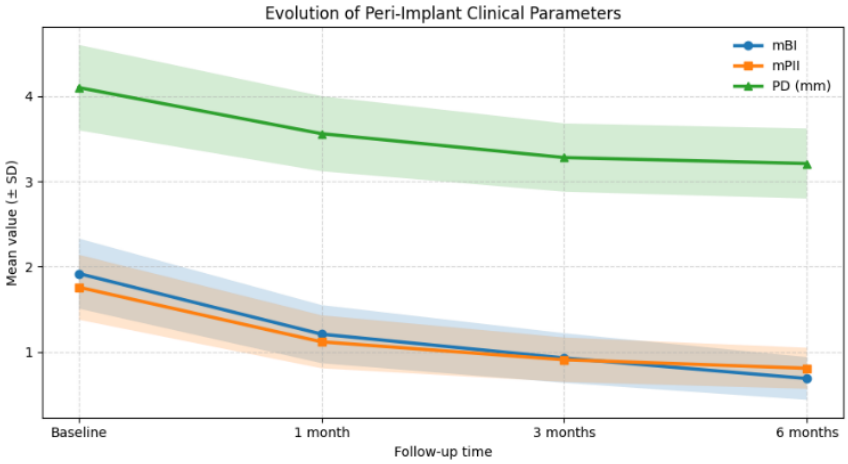

Figure 1. Evolution of peri-implant clinical parameters over a 6-month follow-up. Mean values with standard deviation (shaded areas) for modified Bleeding Index (mBI), modified Plaque Index (mPII), and probing depth (PD) measured at baseline, 1 month, 3 months, and 6 months. All parameters showed a significant reduction over time (repeated-measures ANOVA, $p < 0.05$).

Adverse Events and Compliance

No local or systemic adverse events related to probiotic administration were reported throughout the study duration. Patient adherence to the prescribed probiotic regimen and oral hygiene instructions was high, with an overall compliance rate of 92%, supporting the tolerability and feasibility of this adjunctive therapeutic approach.

Discussions

The present prospective clinical study demonstrates that a 30-day adjunctive probiotic regimen with BioGaia ProDentis is associated with statistically and clinically significant improvements in peri-implant mucosal health in patients diagnosed with peri-implant mucositis. Importantly, these benefits were not limited to the immediate post-treatment period but were sustained for up to six months, suggesting a prolonged biological effect beyond active probiotic administration.

The observed reductions in bleeding on probing and plaque accumulation are indicative of both improved inflammatory control and enhanced biofilm management [12,13]. Bleeding on probing is widely recognized as one of the most reliable clinical indicators of peri-implant mucosal inflammation and a predictor of disease progression [17]. The marked and progressive decrease in mBI values observed in this study, therefore, reflects a meaningful attenuation of inflammatory burden at the peri-implant interface. Likewise, the sustained improvement in mPII suggests that probiotic supplementation may facilitate a more favorable microbial balance, potentially enhancing the effectiveness of routine mechanical plaque control [18].

The modest but statistically significant reduction in probing depth further supports the clinical relevance of the intervention. While peri-implant mucositis is not characterized by bone loss, soft tissue edema and inflammatory infiltration often contribute to increased probing depths [19]. The reduction in PD observed over time likely reflects resolution of inflammation and improved tissue tone rather than true attachment gain, which is nonetheless clinically advantageous in reducing the risk of disease progression.

Several biological mechanisms may explain the clinical outcomes. Lactobacillus reuteri strains are known to produce reuterin, a broad-spectrum antimicrobial compound that inhibits key periopathogens, including Porphyromonas gingivalis, Tannerella forsythia, and Aggregatibacter actinomycetemcomitans. In addition to direct antimicrobial activity, L. reuteri has been shown to exert immunomodulatory effects by downregulating pro-inflammatory cytokines and promoting epithelial barrier function [15,20]. Competitive adhesion to oral surfaces and co-aggregation with pathogenic species further contribute to the stabilization of a commensal-dominated biofilm. These mechanisms are consistent with earlier experimental and clinical observations reported by Bawazir et al., supporting the biological plausibility of the present findings [21].

When compared with existing literature, the peri-implant mucositis resolution rate of 76% observed at six months aligns closely with previously reported outcomes, including a resolution rate of 73.9% in controlled clinical studies evaluating the same probiotic formulation [22]. The magnitude of improvement in bleeding and plaque indices appears comparable, and in some cases superior, to that reported for adjunctive antiseptic therapies such as chlorhexidine. Probiotic therapy avoids well-documented side effects associated with long-term antiseptic use, including tooth staining, taste alteration, and mucosal irritation, thereby potentially improving patient acceptance and adherence.

From a clinical perspective, the findings of this study suggest that probiotic supplementation may represent a valuable adjunct in the non-surgical management of peri-implant mucositis, particularly in patients who exhibit a heightened susceptibility to dysbiosis, reduced manual dexterity, or intolerance to antiseptic agents. The observation that a relatively short course of probiotic administration was sufficient to induce long-lasting clinical benefits further enhances the practicality of this approach in routine implant maintenance protocols.

Nevertheless, certain limitations must be acknowledged. The absence of a control group limits the ability to attribute the observed effects exclusively to probiotic therapy, as improvements may partially reflect enhanced oral hygiene or professional maintenance. The sample size, while adequate to detect overall clinical changes, precluded robust subgroup analyses.

Additionally, the lack of microbiological and immunological assessments restricts direct confirmation of the proposed mechanistic pathways. Despite these limitations, the consistency, magnitude, and durability of the clinical improvements observed provide a strong rationale for future randomized controlled trials incorporating microbiological profiling and biomarker analysis.

Conclusions

Within the limitations of this prospective clinical study, adjunctive administration of BioGaia ProDentis resulted in significant and sustained improvements in peri-implant clinical parameters in patients with peri-implant mucositis. Reductions in bleeding on probing, plaque accumulation, and probing depth were maintained for up to six months following treatment, with a high rate of mucositis resolution and excellent patient tolerance. Probiotic therapy appears to be a safe and effective adjunct to professional mechanical debridement and routine oral hygiene in the management of early peri-implant inflammation. Future investigations should focus on randomized, placebo-controlled, or split-mouth study designs, integrating microbiological and immunological analyses to elucidate the underlying biological mechanisms and optimize clinical protocols.

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