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Clinical effects of local use of probiotics as an adjunct to non-surgical periodontal therapy

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SUMMARY

Introduction Periodontal disease is a chronic inflammatory disease caused by pathologic microorganisms/periopathogens from oral biofilm. Standard periodontal therapy consists of scaling and root planing (SRP). Probiotics can be used as an adjunctive to standard periodontal therapy, since it is known that probiotics can modify pathogenic potential of biofilm by suppressing the colonization of periopathogens.

The aim of this study was to assess the clinical effect of *Bifidobacterium* and *Lactobacillus* probiotic lozenges, probiotic mouthwash, as an adjuvant to SRP in the treatment of initial to moderate chronic periodontitis.

Material and methods Thirty patients with initial to moderate chronic periodontitis were recruited and monitored clinically at baseline (before SRP) and 60 days following SRP. All patients were randomly assigned to experimental group: SRP + probiotic (n = 15) and control group: SRP only (n = 15). The probiotic mouthwash was used twice a day for 60 days. Clinical parameters: the probing pocket depth (PPD), clinical attachment level (CAL) and bleeding on probing (BOP) were measured at baseline and 60th day following SRP. Data were statistically analyzed using the one-way Anova test and SPSS 19 software (IMB Company, New York, U.S.). The Friedman and Mann Whitney tests were used as a post hoc test for intergroup analysis. Statistical significance was set at $p < 0.05$.

Results After 60 days of treatment, the clinical parameters PPD, CAL and BOP were significantly lower in both groups compared to the baseline. In the experimental group, the clinical parameters PPD, CAL and BOP were significantly reduced after 60 days of treatment compared to the initial measurements ($p < 0.05$). In the control group, statistically significant decrease after 60 days of treatment was recorded only for BOP parameter, while there was no statistically significant decrease of PPD and CAL values ($p > 0.05$).

Conclusion The results of the present study demonstrated clinical benefits of adjunctive use of probiotics to SRP in terms of pocket depth reduction in initial to moderate periodontal disease.

Keywords: probiotics; periodontitis; scaling and root planning

INTRODUCTION

Periodontitis is a chronic destructive inflammatory disease of the teeth' supporting tissues caused by a specific microorganisms or group of microorganisms, characterized by a disturbance of homeostatic balance necessary for an efficient host immune response [1, 2]. Even though periodontal disease is considered a multifactorial disease, oral biofilm plays the primary etiological role in the initial development of periodontitis. The golden standard of periodontal therapy is removal of etiological factors, namely oral biofilm. Therefore, the ideal goal of periodontal therapy is decreasing the periodontal pocket depth (PPD) and clinical attachment level (CAL) [3].

To date, ensuring excellent oral hygiene, frequent monitoring for progression or recurrence of periodontal disease and removal of oral biofilm by non-surgical and surgical treatment are considered conventional treatment approaches. Despite widespread clinical advantages of conventional periodontal treatment, it does not always lead to clinical improvement, especially in patients with deep periodontal pockets and patients with comorbidities (diabetes mellitus, obesity, cardiovascular diseases). In these cases, selective use of antibiotics and antiseptics has remained the cornerstone of periodontal treatment [4]. Systemic antibiotic therapy is used to enhance the effects of non-surgical and surgical periodontal treatment and serves to support the host immune system to eliminate subgingival pathogens that remain after SRP. However, antibiotics have many side effects and can cause bacterial resistance. As a result of these limitations, efforts have been made to investigate the use of alternatives, such as probiotics as adjunctive to conventional periodontal treatment [3, 5].

According to the definition of the Food and Agriculture Organization of the United Nations and the World Health Organization, probiotics are living microorganisms (so-called "good" bacteria) that, when applied in adequate quantities, have beneficial effects on the health of a host [6]. Probiotics are natural microorganisms that have great potential in suppressing the reproduction of microorganisms in the oral biofilm without exhibiting side

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effects. Recent studies demonstrated that probiotics have a beneficial effect on human health leading to several new recommendations to encourage the use of probiotics to improve the immune system, including oral health [7, 8, 9].

The effects of probiotics on oral health may be a result of local and/or systemic action. Indirectly, probiotics compete with pathogens for essential nutrients; they can also limit the ability of pathogens to adhere by changing the pH of the medium. By binding to dental tissues, they become part of the biofilm and act as a protective coating for oral tissues against oral diseases. Such biofilm keeps bacterial pathogens away from oral tissue by filling a space that could serve as a niche for pathogens in future [1, 10].

Several studies have examined the adjuvant use of probiotics in the treatment of chronic periodontitis [11–16]. Different outcomes have been observed as a result of probiotic therapy, although most studies suggested beneficial clinical results in the form of decreased PPD, CAL and bleeding on probing (BOP) [17, 18]. However, a study by Morales et al. showed that adjuvant use of probiotics in the treatment of chronic periodontitis does not necessarily lead to an improvement in clinical parameters [11]. Therefore, this randomized placebo-controlled clinical study aimed to evaluate the effect of application of probiotic capsules with *Bifidobacterium* and *Lactobacillus* strain as adjuvants to SRP in the treatment of initial to moderate forms of periodontal disease, measured by clinical parameters (PPD, CAL, BOP).

MATERIAL AND METHODS

The study involved 30 systemically healthy patients, aged 20 to 65 years, with an initial to moderate form of chronic periodontitis who had at least three natural teeth in each quadrant, not counting the third molars. Criteria for exclusion from the study were: presence of systemic diseases, periodontal treatment in the last six months, use of antibiotics or probiotics in the last three months, and pregnant and lactating women. Before the beginning of the study, all subjects were informed in details about the procedures required to perform this study and only those who gave written consent were included in the study.

All patients were randomly assigned to the experimental group: SRP + probiotic (n = 15) or the control group: SRP + placebo (n = 15). Initially, all patients underwent SRP, 7 days prior to the probiotic administration. During that visit, the patients received instructions on maintaining adequate oral hygiene.

Clinical parameters PPD, CAL and BOP were measured at the beginning of the study (7 days following SRP) and on the 60th day (end of study). All clinical measurements were recorded by one investigator, periodontist (T.A.). At the same visit, patients received the instructions of how to use probiotic/placebo capsules. Each patient was given 120 capsules to use twice per day for 60 consecutive days, precisely after waking up and at bedtime following oral hygiene. The content of the capsule would be emptied into 10 ml of distilled water and then vigorously shaken into the oral cavity for 60 seconds, then spit out.

Data were statistically analyzed using one-way ANOVA in SPSS 19 software (IMB Company, New York, USA). The Friedman and Mann-Whitney test were used as post hoc tests for intergroup analysis. The results were presented as mean and standard deviation. Statistical significance was set at $p < 0.05$.

RESULTS

All participants remained until the end of the study and during the study no adverse events were registered. Thirty patients participated in the study, 15 in the experimental group and 15 in the control group. The mean age of the patients in the experimental group was 44.11 ± 4.57 and 43.21 ± 5.43 for the control group. The male/female ratio was approximately the same in both groups. There were 4 smokers in the control group, and 3 in the experimental group (Table 1).

Table 1. Demographic characteristics
Tabela 1. Demografske karakteristike

VARIABLE VARIJABLA	CONTROL GROUP KONTROLNA GRUPA	EXPERIMENTAL GROUP EKSPERIMENTALNA GRUPA	p-value vrednost p
Number of patients Broj pacijenata	15	15	NS NZ
Number of men Broj muškaraca	8	7	NS NZ
Number of women Broj žena	7	8	NS NZ
Number of smokers Broj pušača	4	3	NS NZ
Years Godine	43.21 ± 5.43	44.11 ± 4.57	NS NZ

Significance of the difference between the groups: $p < 0.05$ is significant (bold), NS – is not significant
Značaj razlike između grupa: $p < 0,05$ je značajno (podebljano), NZ – nije značajno

In the control group, PPD at the beginning of therapy was 3.21 mm and at the end 3.20 mm and this difference was not statistically significant. The mean value of CAL was initially 2.84 mm and after two months 2.82 mm and this difference was not statistically significant. The mean value of BOP at the beginning of treatment was 58.42% and at the end 4.13% and this difference were statistically significant (Table 2). In the experimental group, the PPD at the beginning of therapy was 3.51 mm and at the end 3.00 mm and this difference was statistically significant. The mean value of CAL was initially 2.67 mm and after two months 2.33 mm and this difference was statistically significant. The mean value of BOP at the beginning of therapy was 60.72% and at the end 3.48% and this difference were statistically significant (Table 2).

The results demonstrated that topical application of probiotic capsules with *Bifidobacterium* and *Lactobacillus* strain as adjuvants to conventional therapy of periodontal disease lead to a statistically significant decrease in PPD and CAL values in the experimental group ($p < 0.05$), while PPD and CAL values in the control group did not show statistically significant difference ($p > 0.05$). A

Table 2. The comparison of clinical parameters of periodontal disease within and between groups (mean ± SD)
Tabela 2. Poređenje kliničkih parametara parodontopatije unutar i između grupa (srednja vrednost ± SD)

	CONTROL GROUP KONTROLNA GRUPA			EXPERIMENTAL GROUP EKSPERIMENTALNA GRUPA		
	At the beginning of therapy Na početku terapije	Two months later Posle dva meseca	p-value vrednost p	At the beginning of therapy Na početku terapije	Two months later Posle dva meseca	p-value vrednost p
PPD (mm) DPDŽ (mm)						
Mean value Srednja vrednost	3.21 ± 0.52	3.20 ± 0.46	0.58	3.51 ± 0.52	3.00 ± 0.46	0.03*
Mean value of the difference Srednja vrednost razlike		0.01 ± 0.06			0.51 ± 0.06	
CAL (mm) NPE(mm)						
Mean value Srednja vrednost	2.84 ± 0.68	2.82 ± 0.45	0.63	2.67 ± 0.68	2.33 ± 0.45	0.01*
Mean value of the difference Srednja vrednost razlike		0.02 ± 0.23			0.34 ± 0.23	
BOP (%) KPS (%)						
Mean value Srednja vrednost	58.42 ± 5.12	4.13 ± 3.51	0.02*	60.72 ± 9.98	3.48 ± 2.21	0.03*
Mean value of the difference Srednja vrednost razlike		54.29 ± 1.61			57.24 ± 7.77	

Comparison within the group with the Friedman test ($p < 0.05$). Significant values are indicated with star.
Intergroup comparison by Mann Whitney test ($p < 0.05$).
PPD – depth of the periodontal pocket
CAL – level of attachment epithelium
BOP – bleeding during probing
SD – standard deviation
Poređenje unutar grupe korišćenjem Fridmanovog testa ($p < 0,05$). Značajne vrednosti su označene zvezdicom.
Poređenje među grupama pomoću testa Mena i Vitnija ($p < 0,05$).
DPDŽ – dubina parodontalnog džepa
NPE – nivo pričvrsnog epitela
KPS – krvarenje prilikom sondiranja
SD – standardna devijacija

statistically significant difference (decrease) in BOP values was observed in both groups at the end of the treatment (Table 2).

DISCUSSION

The results of our study showed the benefits of adjuvant use of probiotic capsules with *Bifidobacterium* and *Lactobacillus* strain in the treatment of periodontal disease, measured through clinical parameters: PPD, CAL and BOP (Table 2).

The growing prevalence of antimicrobial resistance has encouraged the development of new antimicrobial therapeutic approaches in the treatment of biofilm-related oral diseases [17]. Probiotics are living microorganisms that, when given in adequate amounts, provide a health benefit to the host by preventing the adhesion of pathogenic species, inhibiting bacterial growth, modulating the mucosal immune response, cell proliferation, and improving intestinal barrier integrity. Probiotic species mainly belong to the genera *Bifidobacterium* and *Lactobacillus* and are commonly used to treat various diseases of the gastrointestinal tract, urogenital infections, eczema, and oropharyngeal infections [19]. The main property of probiotics used in the oral cavity is their ability to adhere to the surface of oral structures and colonization [20]. Previous research suggested that probiotics cannot replace destroyed natural flora, but as temporary colonies can help body by performing the same functions as natural flora, giving natural flora enough time to recover [21].

Also, several clinical studies have been conducted with the aim to assess the impact of probiotics in the treatment of oral diseases. It has been shown that probiotics can successfully manipulate the microbiological composition and improve clinical condition of oral diseases such as bad breath, candidiasis and periodontal disease [4, 7, 22–27].

The results of this research are in accordance with the results of the research that examined the activity of *Bifidobacterium lactis* HN019 strain in 41 patients with chronic periodontitis [17]. All subjects were first given total disinfection of the mouth and SRP and they were randomly divided into the two groups: experimental group (probiotics + SRP) and control group (SRP + placebo). Clinical follow-up began at the first visit (before SRP) and then 30 and 90 days of treatment, and in addition to clinical evaluation (PPD and CAL), immunological and microbiological tests were performed. Subjects used probiotic or placebo capsules twice daily for 30 days. The study showed that after 90 days the clinical parameters were improved in the experimental group compared to the control group ie. significantly higher reduction in PPD and CAL was observed in the group that used probiotics [17].

Similarly, Vicario et al. examined the action of *Lactobacillus reuteri* lozenge in systemically healthy subjects, non-smokers, with an initial or moderate form of

periodontitis. Subjects in this double-blind, randomized clinical study were divided into the two groups, experimental and control. The experimental group took one lozenge of *Lactobacillus reuteri* per day for 30 days while the control group used a placebo. Clinical parameters were registered at the beginning and 30 days after the beginning of the treatment. After 30 days, the experimental group showed a statistically significant decrease in all periodontal parameters monitored in this study (plaque index, BOP, PPD). The placebo-treated control group showed no statistically significant changes in periodontal parameters [28].

In a study by Ince et al. the use of probiotic capsules based on *Lactobacillus reuteri* as adjuvant to SRP in the treatment of moderate forms of periodontitis showed excellent results. Subjects used probiotic capsules twice daily for three weeks. As a result of the use of probiotic capsules, there was a decrease in the values of clinical parameters that were monitored: gingival index, plaque index, BOP, PPD and CAL [18].

Contrary to our results are the findings of Morales et al. in whose study the use of probiotic capsules based on *Lactobacillus rhamnosus* did not lead to a significant reduction of clinical parameters (PPD, CAL, plaque index and BOP). Patients used a placebo or probiotic capsules once daily for three months [11].

Data obtained in the literature indicated that different probiotic cultures, as well as the manner and time of their application in the treatment of periodontitis, result in variable outcomes. Despite the literature showing mostly encouraging results, further research is needed to elucidate the potential use of probiotics in the prevention and treatment of periodontitis. A combination of conventional periodontal treatment and probiotics has not yet been introduced into the protocol for the treatment of periodontal patients.

CONCLUSION

The use of probiotic capsules as an adjunct to SRP in the treatment of patients with initial to moderate periodontitis lead to statistically significant improvement in the mean PPD, CAL and BOP values in the observed period of two months. The use of probiotics could bring additional clinical benefits to classical periodontal treatment during the maintenance phase, in terms of reducing PPD, CAL and BOP. However, more studies with larger number of patients and longer observation period in order to assess the ideal method use of probiotics are necessary.

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Klinički efekti lokalne primene probiotika kao adjuvantne mere nehirurškom lečenju parodontopatije

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KRATAK SADRŽAJ

Uvod Parodontopatija je hronična inflamatorna bolest prouzrokovana patološkim mikrorganizmima. Mogući mehanizmi delovanja probiotika u terapiji parodontopatije zasnivaju se na modifikacijama patogenog potencijala mikrobnog biofilma. Probiotici pomažu u stimulisanju rasta zdrave flore i time suzbijaju rast i kolonizaciju patoloških mikroorganizama u toku parodontopatije.
Cilj ove studije je da se proceni klinički efekat primene probiotičkih kapsula sa sojevima *Bifidobacterium* i *Lactobacillus* kao adjuvantima kauzalnoj terapiji parodontopatije (čišćenje i poliranje površine korena zuba, SRP) u lečenju početnog ili umerenog oblika hronične parodontopatije.
Materijal i metode rada Trideset pacijenata sa početnim do umerenim oblikom hronične parodontopatije je regrutovano u ovu studiju i praćeno klinički na početku (pre SRP-a) i 60 dana nakon SRP-a. Svi pacijenti su nasumično raspoređeni u eksperimentalnu grupu: SRP + probiotik (n = 15) ili kontrolnu grupu: SRP + placebo (n = 15). Ispiranje usne duplje rastvorom sa probiotičkim kapsulama je vršeno dva puta dnevno tokom uzastopnih 60 dana. Klinički parametri, dubina parodontalnog džepa (DPDŽ), nivo pripojnog epitela (NPE) i krvarenje prilikom sondiranja (KPS) mereni su na početku lečenja i 60. dana. Podaci su statistički analizirani uz pomoć one-way Anova testa i softvera SPSS 19 (IMB Company, New York, U.S.). Fridmanov test i test Man–Vitni su korišteni kao post hock testovi za međugrupnu analizu. Statistička značajnost je postavljena na $p < 0,05$.
Rezultati Nakon 60 dana terapije, klinički parametri DPDŽ, NPE i KPS bili su značajno niži u obe grupe u poređenju sa početnim vrednostima. U eksperimentalnoj grupi klinički parametri DPDŽ, NPE i KPS su se statistički značajno smanjili posle 60 dana terapije u poređenju sa početnim merenjima ($p < 0,05$). U kontrolnoj grupi statistički značajno smanjenje posle 60 dana terapije zabeleženo je samo za parametar KPS, dok za vrednosti DPDŽ i NPE nije došlo do statistički značajnog smanjenja ($p > 0,05$).
Zaključak Ovo istraživanje je pokazalo da adjuvantna upotreba probiotika u terapiji hronične parodontopatije pruža kliničku korist u smislu smanjenja dubine parodontalnog džepa, nivoa pripojnog epitela i krvarenja prilikom sondiranja.
Ključne reči: probiotici; parodontopatija; obrada parodontalnog džepa

UVOD

Parodontopatija je hronična destruktivna inflamatorna bolest potpornih tkiva zuba uzrokovana specifičnim mikroorganizmom ili grupom specifičnih mikroorganizama koji izazivaju disbiozu, koja se karakteriše poremećajem homeostatske ravnoteže neophodne za efikasan imuni odgovor domaćina, što dovodi do neregulisane upale i gubitka alveolarne kosti [1, 2].

Uprkos tome što se smatra multifaktornom bolešću, oralni biofilm je primarni etiološki faktor nastanka parodontopatije.

Delovanje na primarni etiološki faktor je glavni cilj lečenja parodontopatije. Idealan rezultat terapije parodontopatije predstavlja smanjenje dubine parodontalnog džepa sa smanjenjem nivoa pripojnog epitela [3].

Različiti terapijski modaliteti, koji uglavnom uključuju savete o održavanju oralne higijene i nehirurško terapiju (čišćenje i poliranje površine korena zuba) (SRP), hirurška terapija i u pojedinim slučajevima selektivna primena antibiotika i antiseptika do danas su ostali kamen temeljac terapije parodontopatije [4].

Uprkos široko rasprostranjenim kliničim prednostima, nehirurška terapija parodontopatije ne dovodi uvek do poboljšanja, posebno kod pacijenata sa dubokim parodontalnim džepovima i pacijenta sa komorbiditetima (dijabetes melitus, gojaznost, kardiovaskularne bolesti). U ovim situacijama se adjuvantna primena antibiotika ili probiotika u terapiji može pokazati korisna.

Sistemska antibiotska terapija se koristi za pojačanje delovanja nehirurške i hirurške terapije parodontopatije, služi kao podrška imunom sistemu domaćina za eliminaciju subgingivalnih patogena koji ostaju nakon SRP-a.

Uz SRP, sistemski antibiotici mogu da ponude dodatne pogodnosti; međutim, antibiotici nisu bezopasni lekovi jer je njihova primena praćena pojavom neželjenih efekata i stvaranjem rezistentnih sojeva mikroorganizama. Kao rezultat ovih ograničenja, uloženi su napori da se istraži upotreba probiotika kao druge metode za modulaciju sastava oralnog biofilma u kombinaciji sa SRP-om [3, 5].

Prema definiciji organizacije za hranu i poljoprivredu Ujedinjenih naroda te Svetske zdravstvene organizacije, probiotici su živi mikroorganizmi (tzv. „dobre" bakterije) koji kada se primene u adekvatnoj količini imaju povoljne učinke na zdravlje domaćina [6].

Probiotici su prirodni mikroorganizmi koji imaju veliki potencijal u suzbijanju razmnožavanja mikroorganizama u oralnom biofilmu bez ispoljavanja neželjenih efekata.

Nedavne studije su pokazale da probiotici imaju blagotvoran učinak na zdravlje čoveka, što dovodi do nekoliko novih preporuka za podsticanje upotrebe probiotika u cilju poboljšanja imunog sistema, uključujući i oralno zdravlje [7, 8, 9].

Efekti probiotika na oralno zdravlje mogu proisteći iz lokalnog i sistemskog načina delovanja. Indirektno, probiotici se takmiče sa patogenima za neophodne hranljive sastojke; takođe mogu ograničiti sposobnost adhezije patogena promenom pH sredine. Vezujući se za dentalna tkiva, postaju deo biofilma i deluju kao zaštitna obloga za oralna tkiva protiv oralnih bolesti. Takav biofilm drži bakterijske patogene dalje od oralnog tkiva popunjavanjem prostora koji je mogao da posluži kao niša za patogene u budućnosti [1, 10].

Nekoliko studija je ispitivalo adjuvantnu primenu probiotika u terapiji hronične parodontopatije [11–16].

Različiti ishodi su primećeni kao rezultati terapije probioticima, mada većina studija pokazuje pozitivne kliničke rezultate u vidu smanjenja dubine parodontalnog džepa (DPDŽ), nivoa pripojnog epitela (NPE) i krvarenja prilikom sondiranja (KPS) [17, 18].

Za razliku od studija koje pokazuju pozitivan efekat primene probiotika, studija Moralesa i saradnika je pokazala da adjuvantna primena probiotika u terapiji hronične parodontopatije ne dovodi uvek do poboljšanja kliničkih parametara [11].

Stoga je ova randomizirana placebo kontrolisana klinička studija imala za cilj da proceni klinički efekat (DPDŽ, NPE, KPS) lokalne primene probiotičkih kapsula sa sojevima *Bifidobacterium* i *Lactobacillus* kao adjuvantima kauzalnoj terapiji parodontopatije (SRP) u lečenju početnog do umerenog oblika parodontopatije.

MATERIJAL I METOD RADA

Kriterijumi za učešće u studiji su bili: da su pacijenti muškog ili ženskog pola, starosti od 20 do 65 godina, da imaju najmanje tri prirodna zuba u svakom kvadrantu ne računajući treće molare, da se prethodno nisu lečili od parodontopatije. Kriterijumi za isključenje iz studije su bili: sistemske bolesti, pacijenti koji su u zadnja tri meseca koristili antibiotike ili probiotike, trudnice i dojilje.

Pre samog početka studije svi ispitanici su bili detaljno informisani o procedurama potrebnim za izvođenje ovog istraživanja i samo oni koji su dali pismenu saglasnost su bili uključeni u ovo istraživanje.

U studiji je učestvovalo 30 sistemski zdravih pacijenata sa početnim do umerenim oblikom hronične parodontopatije.

Svi pacijenti su nasumično raspoređeni u eksperimentalnu grupu: SRP + probiotik (n = 15) ili kontrolnu grupu: SRP + Placebo (n = 15). Na početku, svi pacijenti su podvrgnuti SRP-u.

SRP je izveden sedam dana pre početka primene probiotika ili placeba, korišćenjem ručnih i ultrazvučnih instrumenata. U istoj poseti pacijenti su takođe dobili i uputstva o održavanju adekvatne oralne higijene.

Klinički parametri DPDŽ, NPE i KPS mereni su na početku lečenja (sedam dana posle SRP-a) i 60. dana (završetak studije). Sva klinička merenja su zabeležena od strane jednog ispitivača.

Posle registrovanja kliničkih parametara (DPDŽ, NPE, KPS) svakom pacijentu je detaljno objašnjen način primene probiotičkih kapsula ili placeba.

Pacijenti su dobili po 120 kapsula koje su koristili odmah posle obavljanja oralne higijene, dva puta dnevno (posle buđenja i pre spavanja).

Sadržaj kapsule bi ispraznili u 10 ml destilovane vode i zatim energično mućkali usnu duplju 60 sekundi, zatim ispljunuli. Placebo ili probiotičke kapsule sa sojevima *Bifidobacterium* i *Lactobacillus* korišćene su tokom uzastopnih 60 dana.

Podaci su statistički analizirani korištenjem one-way ANOVA testa uz pomoć softvera SPSS 19 (IMB Company, New York, U.S.). Fridmanov i test Man–Vitni korišćeni su kao post hock testovi za međugrupnu analizu. Rezultati su predstavljeni u vidu srednje vrednosti i standardne devijacije. Statistička značajnost je postavljena na $p < 0,05$.

REZULTATI

U studiji je učestvovalo 30 pacijenata – 15 u eksperimentalnoj grupi i 15 u kontrolnoj grupi, koja je primala placebo. Svi učesnici su ostali u studiji do samog završetka studije i nisu registrovani neželjeni događaji. Prosečna starost pacijenata u eksperimentalnoj grupi je bila 44,11 ± 4,57 i 43,21 ± 5,43 za kontrolnu grupu. Procenat muškaraca/žena (8/7) bio je približno jednak u obe grupe. U kontrolnoj grupi je bilo četiri pušača, dok je u eksperimentalnoj bilo tri (Tabela 1).

U kontrolnoj grupi DPDŽ na početku terapije je iznosila 3,21 mm, a na kraju 3,20 mm i ova razlika nije bila statistički značajna. Srednja vrednost NPE je na početku iznosila 2,84 mm, a posle dva meseca 2,82 mm i ova razlika nije bila statistički značajna. Srednja vrednost KPS na početku terapije je iznosila 58,42%, a na kraju 4,13% i ova razlika je bila statistički značajna (Tabela 2).

U eksperimentalnoj grupi grupi DPDŽ na početku terapije iznosila je 3,51 mm, a na kraju 3,00 mm i ova razlika je bila statistički značajna. Srednja vrednost NPE je na početku iznosila 2,67 mm, a posle dva meseca 2,33 mm i ova razlika je bila statistički značajna. Srednja vrednost KPS na početku terapije je iznosila 60,72%, a na kraju 3,48% i ova razlika je bila statistički značajna (Tabela 2).

Rezultati istraživanja su pokazali da lokalna primena probiotičkih kapsula sa sojevima *Bifidobacterium* i *Lactobacillus* kao adjuvantima kauzalnoj terapiji parodontopatije dovodi do statistički značajnog smanjenja vrednosti DPDŽ i NPE kod eksperimentalne grupe ($p < 0,05$), dok se vrednosti DPDŽ i NPE kod kontrolne grupe nisu statistički značajno promenile ($p > 0,05$). Statistički značajno smanjenje vrednosti KPS je primećeno u obe grupe na kraju terapije (Tabela 2).

DISKUSIJA

Ovo istraživanje je imalo za cilj da proceni klinički efekat lokalne primene probiotičkih kapsula sa sojevima *Bifidobacterium* i *Lactobacillus* kao adjuvantima kauzalnoj terapiji parodontopatije u lečenju početnog ili umerenog oblika parodontopatije.

Rezultati istraživanja su pokazali da adjuvantna primena probiotičkih kapsula sa sojevima *Bifidobacterium* i *Lactobacillus* može imati pozitivan efekat u terapiji parodontopatije, odnosno da dolazi do smanjenja vrednosti DPDŽ, NPE i KPS (Tabela 2).

Rastuća prevalencija antimikrobne rezistencije podstaknula je razvoj novih antimikrobnih terapijskih pristupa u lečenju oralnih bolesti povezanih sa biofilmom [17].

Probiotici predstavljaju žive mikroorganizme koji kada se daju u adekvatne količine pružaju zdravstvenu korist za domaćina sprečavanjem adhezije patogenih vrsta, inhibicijom rasta bakterija, modulacijom imunog odgovora sluznice, ćelijske proliferacije i poboljšanjem integriteta crevne barijere. Probiotičke vrste uglavnom pripadaju rodovima *Bifidobacterium* i *Lactobacillus* i obično se koriste za lečenje različitih bolesti gastrointestinalnog trakta, urogenitalnih infekcija, ekcema i orofaringealnih infekcija [19].

Glavno svojstvo probiotika koji se koriste u usnoj šupljini je njihova sposobnost adheriranja za površinu struktura usne šupljine i kolonizacija [20].

Dosadašnja istraživanja naučnika upućuju da probiotici ne mogu zameniti uništenu prirodnu floru, nego kao privremene kolonije mogu pomoći organizmu obavljajući iste funkcije kao prirodna flora, dajući prirodnoj flori dovoljno vremena da se oporavi [21].

Na kliničkom nivou, nekoliko studija je sprovedeno sa ciljem procene uticaja probiotika u lečenju oralnih oboljenja. Pokazalo se da probiotici mogu uspešno manipulisati mikrobiološkim sastavom i poboljšati kliničko stanje kod oralnih oboljenja kao što su neugodan zadah, kandidijaza i bolesti parodoncijuma [4, 7, 22–27].

Rezultati ovog istraživanja su u skladu sa rezultatima istraživanja koje su realizovali Invernici i sar. Oni su ispitivali delovanje soja *Bifidobacterium lactis HN019* na 41 pacijentu sa hroničnom parodontopatijom. Svim ispitanicima je prvo izvršena totalna dezinfekcija usta te SRP. Slučajnim odabirom su podeljeni su u dve grupe. Eksperimentalna grupa: probiotici + SRP i kontrolna grupa: SRP + placebo. Kliničko praćenje započelo je pri prvoj poseti (pre SRP-a) te zatim 30 i 90 dana terapije, a osim kliničke evaluacije (DPDŽ i NPE) vršena su imunološka i mikrobiološka ispitivanja. Ispitanici su koristili kapsule sa probiotikom ili placebom dva puta na dan, kroz 30 dana. Istraživanje je pokazalo da su nakon 90 dana klinički parametri bili poboljšani kod eksperimentalne grupe u poređenju sa kontrolnom grupom. Odnosno, primećena je značajno veća redukcija DPDŽ i NPE kod grupe koja je koristila probiotik [17].

Rezultati studije španskih naučnika Vikarija i saradnika takođe su u skladu sa ovim nalazima. Oni su ispitivali delovanje pastila *Lactobacillus reuteri* kod sistemski zdravih ispitanika, nepušača, s početnim ili umerenim oblikom parodontopatije. Ispitanici su u ovoj, dvostruko slepoj, randomiziranoj kliničkoj studiji, bili podeljeni u dve grupe – eksperimentalnu i kontrolnu. Eksperimentalna grupa je uzimala jednu pastilu *Lactobacillus reuteri* na dan tokom 30 dana, dok je kontrolna koristila placebo. Klinički parametri su registrovani na početku i 30 dana posle početka terapije. Eksperimentalna grupa je posle 30 dana pokazala statistički značajno smanjenje svih parodontoloških parametara praćenih u ovoj studiji (plak indeks, KPS, DPDŽ). Kontrolna grupa tretirana s placebom nije pokazala statistički značajne promene parodontoloških parametara [28].

U studiji Ince i saradnika primena probiotičkih kapsula na bazi *Lactobacillus reuteri* kao adjuvantne mere u terapiji umerenih oblika parodontopatije pokazala je odlične rezultate. Ispitanici su koristili probiotičke kapsule dva puta dnevno tri sedmice. Kao rezultat primene probiotičkih kapsula došlo je do smanjenja vrednosti kliničkih parametara koje su pratili: gingivalnog indeksa, plak indeksa, KPS, DPDŽ i NPE [18].

U suprotnosti sa našim rezultatima su saznanja do kojih su došli Morales i saradnici, u čijem istraživanju primena probiotičkih kapsula na bazi *Lactobacillus rhamnosus* nije dovela do značajnog smanjenja kliničkih parametara (DPDŽ, NPE, plak indeks i KPS). Pacijenti su koristili placebo ili probiotičke kapsule jednom dnevno tri meseca [11].

Podaci do kojih se dolazi u literaturi ukazuju na činjenicu da odabir različitih probiotičkih kultura kao i način i vreme njihove primene u terapiji parodontopatije rezultiraju promenjivim rezultatima.

Uprkos tome što literatura pokazuje uglavnom ohrabrujuće rezultate, potrebna su dodatna istraživanja kako bi se rasvetlila moguća upotreba probiotika u prevenciji i lečenju parodontopatije. Još uvek kombinacija mehaničke terapije (SRP) i probiotika nije uvedena u protokol za lečenje parodontoloških pacijenata.

ZAKLJUČAK

U skladu sa ograničenjima ove studije možemo da zaključimo da adjuvantna upotreba probiotičkih kapsula kao dodatak SRP-u u lečenju pacijenata sa početnim do umerenim oblikom parodontopatije dovodi do statistički značajnog poboljšanja prosečnih vrednosti DPDŽ, NPE i KPS tokom dvomesečnog praćenja. Upotreba probiotika mogla bi doneti dodatne kliničke prednosti klasičnoj terapiji parodontopatije tokom faze održavanja, u smislu smanjenja DPDŽ, NPE i KPS, ali je za potvrdu potrebno više studija sa većim brojem pacijenata i duže praćenje ovih rezultata za procenu idealnog načina primene probiotika.