doi: http://dx.doi.org/10.11606/issn.1679-9836.v103i1e-221034 Rev Med (São Paulo). 2024 Jan-Feb;103(1):e-221034.

Article

The paradoxical role of Lactobacillus on health

O papel paradoxal de Lactobacillus na saúde

Mariana Araujo Mendes Silva[1], Mariella Vieira Pereira Leão[2]

Silva MAM, Leão MVP. The paradoxical role of Lactobacillus on health / *O papel paradoxal de Lactobacillus na saúde.* Rev Med (São Paulo). 2024 Jan-Feb;103(1):e-221034.

ABSTRACT: The genus *Lactobacillus* is part of the normal microbiota, but is related to a variety of human infections, such as dental abscesses, bacteremia, cholecystitis, empyema, endocarditis, meningitis, peritonitis, prosthetic knee infection and pyelonephritis. Paradoxically, there is evidence of the effectiveness of using *Lactobacillus* in the form of probiotics for the prevention and treatment of diarrheal and inflammatory intestinal diseases, bacterial vaginosis, urinary and respiratory tract infections and even tooth decay. The present work aimed to demonstrate and discuss these contradictory roles of the genus *Lactobacillus*. For this, case reports, clinical trials, literature reviews and meta-analyses from the last 30 years were selected, using the keywords: *Lactobacillus*, Probiotics, Dental Caries, Diseases and Health. Different studies have demonstrated that the effects of probiotics can be specific to each strain and that the most effective strain for each clinical condition, its ideal dose, best form of administration and best time of use are still questionable. Furthermore, the existence of a pre-existing comorbidity or susceptible condition in the patient increases the risk of lactobacilli infections. Thus, it was concluded that, only after a careful investigation of the *Lactobacillus* strain and the patient, their oral and general conditions, probiotics containing these microorganisms could be used in a safer, more beneficial and more effective way.

KEY WORDS: *Lactobacillus;* Probiotics; Dental caries and health.

RESUMO: O gênero *Lactobacillus* faz parte da microbiota normal, mas está relacionado a uma variedade de infecções humanas, como abscessos dentários, bacteremia, colecistite, empiema, endocardite, meningite, peritonite, infecção protética do joelho e pielonefrite. Paradoxalmente, há evidências da eficácia da utilização dos *Lactobacillus* sob a forma de probióticos para prevenção e tratamento de doenças diarréicas e inflamatórias intestinais, vaginoses bacterianas, infecções do trato urinário e respiratório e até mesmo cárie dentária. O presente trabalho objetivou demonstrar e discutir esses contraditórios papéis do gênero *Lactobacillus*. Para isso, foram selecionados relatos de caso, ensaios clínicos, revisões da literatura e metanálises, dos últimos 30 anos, utilizando-se as palavras-chaves: *Lactobacillus*, Probiotics, Dental Caries, Diseases and Health. Os diferentes estudos demonstraram que os efeitos dos probióticos podem ser específicos de cada cepa e que a cepa mais efetiva para cada quadro clínico, sua dose ideal, sua melhor forma de administração e melhor momento de utilização ainda são questionáveis. Além disso, a existência de uma comorbidade ou condição suscetível pré existente no paciente aumenta o risco de infecções por lactobacilos. Assim, concluiu-se que, somente após uma investigação cuidadosa da cepa de *Lactobacillus* e do paciente, das suas condições bucais e gerais, os probióticos contendo esses microrganismos poderiam ser utilizados de forma mais segura, benéfica e eficaz.

PALAVRAS CHAVE: *Lactobacillus;* Probióticos; Cárie dentária e saúde.

[1.] Acadêmica de Medicina da Faculdade de Ciências Médicas de São José dos Campos - FCMSJC - Humanitas, São José dos Campos, SP, Brasil. https://orcid.org/0000-0001-6059-9252 - marianaaraujo.ilha@hotmail.com

[2.] Professora Adjunta da Faculdade de Ciências Médicas de São José dos Campos - FCMSJC - Humanitas, São José dos Campos, SP, Brasil. Professora Adjunta III da Universidade de Taubaté – UNITAU, Taubaté, SP, Brasil. https://orcid.org/0000-0003-1949-3207 - mariella.leao@humanitas.edu.br

Correspondence: Mariana Araujo Mendes Silva, rua Pedro Ribeiro Pontes, 222, Reino, CEP 11630-000, Ilhabela, SP, Brasil.

INTRODUCTION

Lactobacillus is a genus of facultative anaerobic, Gram-positive, rod-shaped bacteria frequently found in the resident oral, intestinal and vaginal microbiota[1].

The genus *Lactobacillus* may also be associated with several pathological conditions such as, dental caries and abscesses, bacteremia, cholecystitis, empyema, endocarditis, meningitis, peritonitis, prosthetic knee infection and pyelonephritis[2]. The role of lactobacilli in dental caries has been investigated for a long time, and high counts of these microorganisms are often correlated with high cariogenic indices[3].

Lactobacillus is a probiotic microorganism found in freeze-dried form or in fermented foods that can alleviate gastrointestinal disorders, bacterial and viral infections, prevent or alleviate allergies and atopic diseases[4]. The concept of probiotic is attributed to live microorganisms that promote health benefits for the host when administered in appropriate quantities[5].

Probiotics can be used in the prevention and treatment of various diarrheal and inflammatory bowel diseases, bacterial vaginosis, urinary and respiratory tract infections, eczema, necrotizing enterocolitis and gastroenteritis[6]. Furthermore, the consumption of foods with *Lactobacillus* can reduce the prevalence and quantity of the genus *Candida* in the oral cavity[7] and inhibit other cariogenic microorganisms, demonstrating a possible protective role against the development of oral thrush and caries[8].

As the literature points to different and contradictory roles of *Lactobacillus*, the survey of different studies and the analysis of the conditions under which each one was performed are fundamental to choose the best form of administration of probiotics and reach health instead of disease.

METHODS

This is a narrative review of the literature in which the PubMed database was used to survey and select case reports, clinical trials, literature reviews and meta-analyses from the last 30 years using the keywords: *Lactobacillus*, Probiotics, Dental Caries, Diseases and Health. The "full text" and "English language" filters were used. Initially, 918 works were found, of which 49 were selected according to the objective of the study.

RESULT AND DISCUSSION

Benefits of *Lactobacillus*

Some strains of the genus *Lactobacillus* may play an important role in maintaining host health by stimulating natural immunity and contributing to the balance of the microbiota in various habitats, such as the gastrointestinal and genitourinary tracts and the oral cavity. Therefore, the use of lactobacilli as probiotics has been suggested to preserve microbial homeostasis in these locations[8].

Several studies have provided evidence of the effectiveness of probiotics for the prevention and treatment of various diarrheal and inflammatory bowel diseases, bacterial vaginosis, urinary and respiratory tract infections, and tooth decay, in addition to promoting growth in healthy, sick or malnourished children[9].

Shu et al.[10] reported that piglets treated with probiotics showed a reduction in diarrhea caused by Rotavirus and *Escherichia coli* and a concomitant increase in antibody titers against these pathogens in the gastrointestinal tract. Pereira et al.[11] studied the action of *Lactobacillus plantarum* and *Lactobacillus fermentum* in vitro against EPEC and ETEC strains of *E. coli* and observed an inhibition in the adherence of these microorganisms, probably caused by the action of bacteriocins, as the pH remained constant.

Khazaie et al.[12] used genetically modified strains of *Lactobacillus acidophilus* (deficient in lipoteichoic acid) and observed their ability to regulate inflammation and promote the regression of colon polyps in animal models.

Reid and Burton[13] observed that four species of the genus *Lactobacillus* reduced the colonization of *Staphylococcus aureus* in vaginal epithelial cells in vitro, through the production of acids and consequent reduction in pH, suggesting the use of these microorganisms to promote balance in the urogenital area.

Oral administration of a specific strain of *Lactobacillus pentosus* (b240) differently regulated the expression of antiviral genes in the lungs of mice infected with influenza virus A (H1N1)[14].

The administration of probiotics in the pediatric population has been associated with a low risk of adverse events and was generally well tolerated. The best documented efficacy is in the treatment of gastroenteritis and prevention of diarrhea associated with antibiotics and *Clostridium difficile*[15].

In the intensive care unit, probiotics appear to offer benefits not only in antibiotic-associated diarrhea, but also in ventilator-associated pneumonia and necrotizing enterocolitis. With increasing rates of antibiotic resistance and decreasing development of new antibiotics, greater attention has been given to non-antibiotic approaches for the prevention and treatment of nosocomial infections[16].

Probiotics have also been recommended to reduce uropathogenic colonization in the urinary tract and manage both infection and antibiotic resistance[17]. The role of these agents in the prevention of allergies has been studied, finding a moderate benefit of probiotics in the prevention of eczema, with the most consistent effects observed with a combined perinatal intervention in infants at high risk of allergic disease due to family predisposition[18].

The use of probiotics associated with vitamin D supplementation has demonstrated the most diverse benefits, such as: reduced disease severity, improved metabolic parameters, especially insulin sensitivity, dyslipidemia and inflammation, improved mental health, among others[19]. Still in relation to mental health, Fond et al.[20] reported benefits of probiotics in conditions such as major depression (MD) and schizophrenia.

Probiotics have also emerged as an alternative to combat oral diseases[21]. The concept of enriching the oral microbiota with "favorable" species follows the paradigm that maintaining a

healthy microbiota is more efficient than eliminating pathogenic microbiota[22].

It was observed that the consumption of probiotic foods containing *Lactobacillus* reduced the counts of yeast of the genus *Candida* in the oral cavity of adults or older adults, contributing to the control of oral thrush[6,7]. According to a work by Leão et al., 2018[23], the consumption of *L. rhamnosus*, mainly preventively, reduced the development of candidiasis in immunosuppressed animals. The *Lactobacillus salivarius* reduced the count of *Porphyromonas gingivalis*, and *L. reuteri* reduced gengivitis and bacterial plaque scores[24].

With regard to dental caries, it has been demonstrated that different species and different strains of *Lactobacillus* can inhibit cariogenic bacteria, such as *Streptococcus mutans* in the oral cavity[25]. Nikawa et al.[26], developed a study with young adult women who consumed bovine milk fermented with *Lactobacillus reuteri* and observed a significant reduction in *S. mutans* counts, resulting in a reduced risk of tooth decay.

An in vivo study suggested that the species *Lactobacillus rhamnosus* GG could inhibit the colonization of *Streptococcus mutans* in the oral cavity, thus reducing the risk of caries. In this study, 74 young adults used cheese enriched with the probiotic species for three weeks and showed a significant reduction of 20% in *Streptococcus mutans* counts and 27% in yeast counts[27].

Chuang et al.[28] performed a study of 78 patients aged between 20 and 26 years, with oral administration of 33 tablets of *L. paracesei* GMNL three times a day for two weeks. *S. mutans* counts were performed at the beginning, after using the medicine and two weeks after the end of the medicine, and a significant reduction in these microorganisms was observed in the last count.

Cagetti et al.[29] performed a systematic review on the role of probiotics (many of which contain *Lactobacillus*) in preventing caries, and found that in three thirds of the 23 selected studies, probiotics demonstrated the ability to reduce *S. mutans* counts in saliva and/or plaque. However, risk factors for the development of the disease were addressed in most studies, whereas the development of carious lesions was investigated only in three.

Even though various evidence demonstrates the benefits of probiotics in different diseases, the quality of the evidence, the specificity of the strains and the best way to administer it still limit the routine prescription of probiotics in clinical practice.

Lactobacillus and infection

Despite the possible benefits of *Lactobacillus* in preventing tooth decay, its association with the development of tooth decay has been known for several decades. Baca et al[30], when examining 95 children aged 6-7 years, observed high *Lactobacillus* counts correlated with a high risk of developing caries. The authors suggested that this association could represent an important complementary analysis as a predictor of cavities in children[31].

While studying 65 deep carious lesions, Martin et al.[21] observed that the species *Lactobacillus acidophilus* was numerically dominant. Other species such as *Lactobacillus paracasei*, *Lactobacillus rhamnosus* and *Lactobacillus fermentum* were also present in the samples, although in smaller quantities. In turn, Teanpaisan et al.[32] and Piwat et al.[33] found a predominance of the species *Lactobacillus salivarius* in cavities of preschool children. The authors observed that acid production varied according to the species and microbial strain, and *lactobacillus* strains isolated from individuals at high risk of caries were more acidogenic.

The production of organic acids by *Lactobacillus* is very important in the decalcification of the dental matrix[34] and the assessment of its aciduric capacity and its other virulence factors also allows a correlation with the frequency and activity of caries[35]. *Lactobacillus* may also present resistance to the most common antimicrobial agents. This implies the need for periodic antimicrobial susceptibility tests of caries pathogens, avoiding the selection of multi-resistant cariogenic organisms[3]. Smiline et al.[36] found high percentages of *Lactobacillus sp.* in different types of cavities, and approximately 47.3% of the isolates showed resistance to several antimicrobials.

In addition to caries, cases of other infections caused by the *Lactobacillus* genus have been reported, some severe, such as endocarditis[37-5]. A case report by Nishijima et al., 2012 revealed a case of infectious endocarditis caused by *Lactobacillus acidophilus* in a patient taking long-term steroids for autoimmune hepatitis. The authors suggested that the origin of the pathogens could be the patient's poorly treated carious lesion[5]. One study demonstrated that in patients with bacteremia caused by *L. rhamnosus*, 66% of cases were associated with immunosuppression and 83% with the use of catheters[38].

Although rare, cases of cholecystitis associated with *Lactobacillus* are also reported in the literature. Chery et al., 2013 reported a case of a patient diagnosed with cholecystitis and ascending cholangitis caused by vancomycin-resistant *Lactobacillus fermentum*. The microorganism was identified in the cholecystostomy aspirate and blood culture and the outcome was the development of septic shock and multiple organ dysfunction, leading to the patient's death[39]. Another report presented a case of perforated cholecystitis with purulent peritonitis in which *Lactobacillus plantarum* was isolated from bile and peritoneal fluid cultures of a patient with underlying disease[40].

Species of lactobacilli have also been associated with cases of empyema[41]. There is a report in the literature of a lung transplant recipient infected with the human immunodeficiency virus who developed empyema after receiving probiotics containing *L. rhamnosus* GG[42]. According to the authors, lung and heart transplant recipients at the study institution routinely received *Lactobacillus* probiotics during hospitalization for prophylaxis against *Clostridium difficile* diarrhea. However, after the introduction of the *L. rhamnosus* GG probiotic, *Lactobacillus* was found to cause the disease in two cases of bacteremia, in addition to the reported case of empyema.

Robin et al., 2010, described a case of meningitis caused by *L. rhamnosus* in a child undergoing allogeneic hematopoietic stem cell transplantation for acute leukemia. However, the infection was not associated with the use of probiotics or colonic anomalies, thus highlighting the risk of lactobacilli infection in

immunocompromised patients even without probiotic intake[43].

With regard to peritonitis, the association with different species of the genus *Lactobacillus* has already been described, such as *L. fermentum*, *L. paracasei*, *L. plantarum* and *L. rhamnosus*. Neef et al., 2003 reported a case of recurrent peritonitis related to continuous ambulatory peritoneal dialysis caused by *Lactobacillus* in which the patient was receiving prolonged treatment with vancomycin intraperitoneally[2, 44].

Chazan et al., 2008, also presented a case of bacteremia and pyelonephritis caused by *Lactobacillus jensenii* in a patient with urolithiasis[45]. In a rare case report in the literature of knee prosthesis infection caused by *Lactobacillus*, the authors warned about the risk of this type of infection with the oral intake of certain foods and probiotic supplements[46].

Studies sought to characterize the virulence of some strains of *Lactobacillus* that cause infections, and reported that the high capacity for biofilm formation favored their pathogenicity, which would be determined by characteristic genetic variations[47].

Table 1 lists different studies and cases in which microorganisms of the genus *Lactobacillus* played a pathogenic role and presents information on the possible use of probiotics by patients and the existence of comorbidities.

Table 1: Publications with reports of infections caused by *Lactobacillus* and information from patient(s) about probiotic consumption or the existence of comorbidities.

AUTHORS	PATHOLOGY	ETIOLOGY	PROBIOTIC/STRAIN	COMORBIDITIES
Nishijima et al.[5]	Endocarditis	*L. acidophilus*	-	Carious lesion
Chery et al.[39]	Cholecystitis and Cholangitis	*L. fermentum*	*L. acidophilus*	-
Luong et al.[42]	Empyema	*L. rhamnosus* GG	*L. rhamnosus* GG	HIV infection
Robin et al.[43]	Meningitis	*L. rhamnosus*	-	Acute leukemia
Neef et al.[44]	Peritonitis	*L. paracasei*	-	Severe kidney disease
Chazan et al.[45]	Pyelonephritis	*L. jensenii*	-	Breast lymphoma Diabetes Arterial hypertension
Hubbard et al.[48]	Fasciitis	*L. acidophilus*	-	Diabetes
Baca et al. [9] Martin et al.[21] Teanpaisan et al.[32] Piwat et al.[33]	Dental cavity	*Lactobacillus* spp.	-	-

Source: prepared by the authors

FINAL CONSIDERATIONS

Given the frequent demonstrations of benefits from consuming probiotic foods, their use in different diseases could reduce the cost of conventional therapy and prevention programs, encouraging the implementation of a healthy diet instead of the administration of medications[49].

Although various studies have been performed, uncertainties regarding the benefits of *Lactobacillus* still remain, showing the need for further scientific research to find the most appropriate use of these probiotic microorganisms for improved oral and general health.

When analyzing the conditions under which the various studies were developed, the effects of probiotic microorganisms

may be specific to each strain. Therefore, a beneficial action related to one strain cannot be attributed to another, even if they are from the same species. It would be necessary to determine the most effective strain with the best adherence and permanence in the desired location that would provide the best results in relation to competition with pathogenic microorganisms. Furthermore, knowledge of the ideal dose, the best form of administration and duration, as well as the best time to use a probiotic microorganism is still desirable in order to maximize its benefits and make its prescription unquestionable.

Once established in the host's locations, there may be a mechanism by which lactobacilli present in probiotics can spread and cause infections. According to Luong et al.[42], after *Lactobacillus* colonization in the gastrointestinal tract, its microaspiration or translocation through the intestinal mucosa could occur, reaching the final organ through the bloodstream. Although only one study in the present work confirmed that probiotic food used by the patient was the source of the lactobacilli causing the infection, this association may be underestimated. Probiotic foods have become more accessible and varied, and information on previous use by the patient can hardly be obtained by the physician. Furthermore, as *Lactobacillus* is part of the normal microbiota, regardless of the original source of this microorganism, the need for further investigation into the source of the infection may be ruled out.

The studies selected in the present work also suggest that the existence of a comorbidity or pre-existing susceptible condition increases the risk of lactobacilli infection, casting doubt on the safe use of probiotic foods in these patients. According to Rossi et al.[47], genetic variations characteristic of probiotic strains of *Lactobacillus* were related to their pathogenic capacity. Therefore, the authors suggested a periodic reassessment of the genetic stability of these strains to ensure that only non-pathogenic variants are administered to vulnerable individuals, preventing them from becoming a risk in these patients.

Thus, only after a more solid knowledge about the benefits of probiotics, a careful investigation of the *Lactobacillus* strain, the patient and his/her oral and general conditions, could probiotics containing these microorganisms be used in a safer, more beneficial and more effective way.

Acknowledgements: We thank Professor Gerusa Correia do Amaral Ribeiro, from Centro Universitário São Lucas, for her collaboration with information regarding oral health and librarian Denise Carvalho da Silva Serrano for all the technical help.

Author participation: Mariana Araujo Mendes Silva: Writing and submission. Mariella Vieira Pereira Leão: Guidance, correction and writing.

REFERENCES

1. Dal Bello F, Hertel C. Oral cavity as natural reservoir for intestinal lactobacilli. Syst Appl Microbiol. 2006;29(1): 69-76. Doi: https://doi.org/10.1016/j.syapm.2005.07.002
2. Goldstein EJ, Tyrrell KL, Citron DM. Lactobacillus species: taxonomic complexity and controversial susceptibilities. Clin Infect Dis. 2015;60 (Suppl.2):S98-107. Doi: https://doi.org/10.1093/cid/civ072
3. Dal Bello F, Hertel C. Oral cavity as natural reservoir for intestinal lactobacilli. Syst Appl Microbiol. 2006;29(1):69-76. Doi: https://doi.org/10.1016/j.syapm.2005.07.002
4. Yagi S, Akaike M, Fujimura M, Ise T, Yoshida S, Sumitomo Y,et al. Infective endocarditis caused by lactobacillus. Intern Med. 2008;47:1113-6. Doi: https://doi.org/10.2169/internalmedicine.47.0744
5. Nishijima T, Teruya K, Yanase M, Tamori Y, Mezaki K, Oka S. Infectious endocarditis caused by lactobacillus acidophilus in a patient with mistreated dental caries. Intern Med. 2012;51:1619-21. Doi: https://doi.org/10.2169/internalmedicine.51.7294
6. Yagi S, Akaike M, Fujimura M, Ise T, Yoshida S, Sumitomo Y, Matsumoto T. Infective endocarditis caused by lactobacillus. Intern Med. 2008;47:1113-6. Doi:https://doi.org/10.2169/internalmedicine.47.0744
7. Nishijima T, Teruya K, Yanase M, Tamori Y, Mezaki K, Oka S. Infectious endocarditis caused by Lactobacillus acidophilus in a patient with mistreated dental caries. Intern Med. 2012;51:1619-21. Doi: https://doi.org/10.2169/internalmedicine.51.7294
8. Pradeep K, Kuttappa MA, Prasana KR. Probiotics and oral health: an update. SADJ. 2014 Feb;69(1):20-4.
9. Minocha A. Probiotics for preventive health. Nutr Clin Pract. 2009;24:227-41. Doi: https://doi.org/10.1177/0884533608331177
10. Shu Q, Qu F, Gill HS. Probiotic treatment using Bifidobacterium lactis HN019 reduces weanling diarrhea associated with rotavirus and Escherichia coli infection in a piglet model. J Pediatr Gastroenterol Nutr. 2001;33:171-7. Doi: https://doi.org/10.1097/00005176-200108000-00014
11. Pereira CAS, Luchese RH, Valadão RC. Potencial probiótico de linajes de Lactobacillus plantarum y Lactobacillus fermentum. Alimentaria. 2004;53-9.
12. Khazaie K, Zadeh M, Khan MW, Bere P, Gounari F, Dennis K, Blatner NR, Owen JL, Klaenhammer TR, Mohamadzadeh M. Abating colon cancer polyposis by Lactobacillus acidophilus deficient in lipoteichoic acid. Proc Natl Acad Sci U S A 2012; 109:10462-7. Doi: https://doi.org/10.1073/pnas.1207230109
13. Burton JP, Reid G. Evaluation of the bacterial vaginal flora of 20 postmenopausal women by direct (Nugent score) and molecular (polymerase chain reaction and denaturing gradient gel electrophoresis) techniques. J Infect Dis. 2002;186:1770-80. Doi: https://doi.org/10.1086/345761
14. Kiso M, Takano R, Sakabe S, Katsura H, Shinya K, Uraki R, Watanabe S, Saito H, Toba M, Kohda N, Kawaoka Y. Protective efficacy of orally administered, heat-killed Lactobacillus pentosus b240 against influenza A virus. Sci Rep 2013;3:1563. Doi: https://

doi.org/10.1038/srep01563

15. Depoorter L, Vandenplas Y. Probiotics in Pediatrics. A Review and Practical Guide. Nutrients. 2021;13(7):2176. Doi: https://doi.org/10.3390/nu13072176

16. Morrow LE, Gogineni V, Malesker MA. Probiotic, prebiotic, and synbiotic use in critically ill patients. Curr Opin Crit Care. 2012;18(2):186-91. Doi: https://doi.org/10.1097/MCC.0b013e3283514b17

17. Toh SL, Boswell-Ruys CL, Lee BSB, Simpson JM, Clezy KR. Probiotics for preventing urinary tract infection in people with neuropathic bladder. Cochrane Database Syst Rev. 2017;9(9):CD010723. Doi: https://doi.org/10.1002/14651858.CD010723.pub2

18. West CE. Probiotics for allergy prevention. Benef Microbes. 2016;7(2):171-9. Doi: https://doi.org/10.3920/BM2015.0073

19. Abboud M, Rizk R, AlAnouti F, Papandreou D, Haidar S, Mahboub N. The health effects of vitamin D and Probiotic Co-Supplementation: a systematic review of randomized controlled trials. Nutrients. 2020;13(1):111. Doi: https://doi.org/10.3390/nu13010111

20. Fond GB, Lagier JC, Honore S, Lancon C, Korchia T, Sunhary De Verville PL, Llorca PM, Auquier P, Guedj E, Boyer L. Microbiota-Orientated treatments for major depression and schizophrenia. Nutrients.2020;12(4):1024. Doi: https://doi.org/10.3390/nu12041024

21. Martin FE, Nadkarni MA, Jacques NA, Hunter N. Quantitative microbiological study of human carious dentine by culture and real-time PCR: association of anaerobes with histopathological changes in chronic pulpitis. J Clin Microbiol 2002;40:1698-704. Doi: https://doi.org/10.1128/jcm.40.5.1698-1704.2002

22. He X, Lux R, Kuramitsu HK, Anderson MH, Shi W. Achieving probiotic effects via modulating oral microbial ecology. Adv Dent Res 2009; 21:53-6. https://doi.org/10.1177/0895937409335626

23. Leão MVP, Tavares TAA, Gonçalves e Silva CR, dos Santos SSF, Junqueira JC, de Oliveira LD, Jorge AOC. Lactobacillus rhamnosus intake can prevent the development of candidiasis. Clin Oral Investig. 2018;22(7):2511-8. Doi: https://doi.org/10.1007/s00784-018-2347-8

24. Twetman S, Keller MK. Probiotics for caries prevention and control. Adv Dent Res. 2012;24:98-102. Doi: https://doi.org/10.1177/0022034512449465

25. Krasse P, Carlsson B, Dahl C, Paulsson A, Nilsson A, Sinkiewicz G. Decreased gum bleeding and reduced gingivitis by the probiotic Lactobacillus reuteri. Swed Dent J. 2006;30:55-60.

26. Nikawa H, Makihira S, Fukushima H, Nishimura H, Ozaki Y, Ishida K, Darmawan S, Hamada T, Hara K, Matsumoto A, Takemoto T, Aimi R. Lactobacillus reuteri in bovine milk fermented decreases the oral carriage of mutans streptococci. Int J Food Microbiol. 2004;95:219-23. Doi: https://doi.org/10.1016/j.ijfoodmicro.2004.03.006

27. Ahola AJ, Yli-Knuuttila H, Suomalainen T, Poussa T, Ahlström A, Meurman JH, Korpela R. Short-term consumption of probiotic-containing cheese and its effect on dental caries risk factors. Arch Oral Biol. 2002;47:799-804. Doi: https://doi.org/10.1016/S0003-9969(02)00112-7

28. Chuang LC, Huang CS, Ou-Yang LW, Lin SY. Probiotic Lactobacillus paracasei effect on cariogenic bacterial flora. Clin Oral Investig. 2011;15(4):471-6. Doi: https://doi.org/10.1007/s00784-010-0423-9

29. Cagetti MG, Mastroberardino S, Milia E, Cocco F, Lingström P, Campus G. The use of probiotic strains in caries prevention: a systematic review. Nutrients. 2013;5(7):2530-50. Doi: https://doi.org/10.3390/nu5072530

30. Baca P, Parejo E, Bravo M, Castillo A, Liébana J. Discriminant ability for caries risk of modified colorimetric tests. Med Oral Patol Oral Cir Bucal. 2011;16:978-83. Doi: https://doi.org/10.4317/medoral.17358

31. van Palenstein Helderman WH, Mikx FH, Van't Hof MA, Truin G, Kalsbeek H. The value of salivary bacterial counts as a supplement to past caries experience as caries predictor in children. Eur J Oral Sci. 2001;109:312-5. Doi: https://doi.org/10.1034/j.1600-0722.2001.00080.x

32. Teanpaisan R, Thitasomakul S, Piwat S, Thearmontree A, Pithpornchaiyakul W, Chankanka O. Longitudinal study of the presence of mutans streptococci and lactobacilli in relation to dental caries development in 3-24 month old Thai children. Int Dent J. 2007;57:445-51. Doi: https://doi.org/10.1111/j.1875-595X.2007.tb00148.x

33. Piwat S, Teanpaisan R, Thitasomakul S, Thearmontree A, Dahlén G. Lactobacillus species and genotypes associated with dental caries in thai preschool children. Mol Oral Microbiol. 2010;25:157-64. Doi: https://doi.org/10.1111/j.2041-1014.2009.00556.x

34. Byun R, Nadkarni MA, Chhour KL, Martin FE, Jacques NA, Hunter N. Quantitative analysis of diverse Lactobacillus species present in advanced dental caries. J Clin Microbiol. 2004;42:3128-36. Doi: https://doi.org/10.1128/jcm.42.7.3128-3136.2004

35. Palomer R, Leonor. Caries dental en el niño: Una enfermedad contagiosa. Rev Chil. Pediatr.[online]. 2006;77:56-60. Doi: http://dx.doi.org/10.4067/S0370-41062006000100009

36. Smiline GA, Pandi SK, Hariprasad P, Raguraman R. A preliminary study on the screening of emerging drug resistance among the caries pathogens isolated from carious dentine. Indian J Dent Res. 2012;23:26-30. Doi: https://doi.org/10.4103/0970-9290.99033

37. Yagi S, Akaike M, Fujimura M, Ise T, Yoshida S, Sumitomo Y, Ikeda Y, Iwase T, Aihara K, Azuma H, Kurushima A, Ichikawa Y, Kitagawa T, Kimura T, Nishiuchi T, Matsumoto T. Infective endocarditis caused by lactobacillus. Intern Med. 2008; 47: 1113-6. Doi: https://doi.org/10.2169/internalmedicine.47.0744

38. Gouriet F, Million M, Henri M, Fournier PE, Raoult D. Lactobacillus rhamnosus bacteremia: an emerging clinical entity. Eur J Clin Microbiol Infect Dis. 2012;31(9):2469-80. Doi: https://doi.org/10.1007/s10096-012-1599-5

39. Chery J, Dvoskin D, Morato FP, Fahoum B. Lactobacillus fermentum, a pathogen in documented cholecystitis. Int J Surg Case Rep. 2013;4(8):662-4. Doi: https://doi.org/10.1016/j.ijscr.2013.04.034

40. Tena D, Martínez NM, Losa C, Fernández C, Medina MJ, Sáez-Nieto JA. Acute acalculous cholecystitis complicated with peritonitis caused by Lactobacillus plantarum. Diagn Microbiol Infect Dis. 2013;76(4):510-2. Doi: https://doi.org/10.1016/j.diagmicrobio.2013.03.018

41. Civen R, Jousimies-Somer H, Marina M, Borenstein L, Shah H, Finegold SM. A retrospective review of cases of anaerobic empyema and update of bacteriology. Clin Infect Dis. 1995;20(suppl. 2):S224-9.

Doi: https://doi.org/10.1093/clinids/20.Supplement_2.S224

42. Luong ML, Sareyyupoglu B, Nguyen MH, Silveira FP, Shields RK, Potoski BA, Pasculle WA, Clancy CJ, Toyoda Y. Lactobacillus probiotic use in cardiothoracic transplant recipients: a link to invasive lactobacillus infection? Transpl Infect Dis. 2010;12(6):561-4. Doi https://doi.org/10.1111/j.1399-3062.2010.00580.x

43. Robin F, Paillard C, Marchandin H, Demeocq F, Bonnet R, Hennequin C. Lactobacillus rhamnosus meningitis following recurrent episodes of bacteremia in a child undergoing allogeneic hematopoietic stem cell transplantation. J Clin Microbiol. 2010;48(11):4317-9. Doi: https://doi.org/10.1128/JCM.00250-10

44. Neef PA, Polenakovik H, Clarridge JE, Saklayen M, Bogard L, Bernstein JM. Lactobacillus paracasei continuous ambulatory peritoneal dialysis-related peritonitis and review of the literature. J Clin Microbiol. 2003;41(6):2783-4. Doi: https://doi.org/10.1128/jcm.41.6.2783-2784.2003

45. Chazan B, Raz R, Shental Y, Sprecher H, Colodner R. Bacteremia and pyelonephritis caused by lactobacillus jensenii in a patient with urolithiasis. Isr Med Assoc J. 2008;10(2):164-5.

46. Bennett DM, Shekhel T, Radelet M, Miller MD. Isolated lactobacillus chronic prosthetic knee infection. Orthopedics. 2014;37(1):e83-86. Doi: https://doi.org/10.3928/01477447-20131219-22

47. Rossi F, Amadoro C, Gasperi M, Colavita G. Lactobacilli infection case reports in the last three years and safety implications. Nutrients. 2022;14(6):1178. Doi: https://doi.org/10.3390/nu14061178

48. Hubbard J, Jariwala B, Hill A, Gega A, Palesty JA. A new bacterium, *Lactobacillus acidophilus*, causing necrotizing fasciitis. Am Surg. 2018;84(2):e61-e63.

49. Pradeep K, Kuttapa MA, Prassana Rao. Probiotics and oral health: an update. Biol Biomed Rep 2012;2:246-52.

Received: 2024, January 12
Accepted: 2024, April 09