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Probiotic supplementation in dental caries: is it possible to replace conventional treatment?

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Abstract

Background: Probiotic supplementation alters oral microbiota composition and could reduce the risk or treat oral cavity diseases, such as dental caries, which are considered a public health problem.

Aim: To summarize the therapeutic effects of probiotics in caries and to verify whether this intervention is capable of replacing conventional treatment in human beings.

Methods: The search of the studies was carried out in the PubMed database in October 2017, without limiting the publication period. The keyword combination used was "Probiotics" and "Dental caries." Forty-two original articles that evaluated the effect of probiotic supplementation on caries treatment in humans were included in the study.

Results: Most of the studies evaluated bacteria of the genus *Lactobacillus*. The main therapeutic effects are related to the reduction of the *Streptococcus mutans* oral count, increased *Lactobacillus* oral count, and reduction in the incidence of caries. Evidence on the therapeutic effects of the *Bifidobacterium* and *Streptococcus* genres is scarce and conflicting, making it difficult to recommend them for use in clinical practice. Only a few studies administered probiotics without conventional treatments, such as fluoride. Although probiotic supplementation presented interesting properties, the therapeutic effects are more pronounced when probiotic and fluoride are applied together.

Conclusion: Probiotics, especially of the *Lactobacillus* genus, can be used as adjuvants, but cannot replace the conventional treatments of caries.

Keywords: Probiotic, Dental caries, Treatment, Microorganism, Bacteria

Background

Probiotics are considered "live microorganisms that, when administered in adequate amounts, confer health benefits on the host" [1, 2]. One of the main probiotic health claims is the positive change in microbiota composition [3, 4], traditionally investigated in regard to intestinal health [5–9]. However, there is evidence that probiotic therapy also alters oral microbiota and reduces the risk or could be used in the treatment of oral cavity diseases [10–12]. Briefly, the mechanisms proposed for probiotic actions consist of adhesion to the tooth surface and competition with cariogenic bacteria to reduce their growth [13] and the modulation of microbiota composition, thereby promoting oral health [14]. When in high amounts in the oral cavity, beneficial bacteria, such as those belonging to the *Lactobacillus* genus, inhibit the growth of pathogenic bacteria, such as cariogenic streptococci, preventing the development of dental caries [14, 15]. This is a multifactorial disease caused by the interaction of dietary sugar, dental biofilm, and the host's dental tissue. Specific microorganisms, such as *Streptococcus mutans*, produce acid after consuming sugar, and this leads to the demineralization of dental enamel [16].

Dental caries is one of the most common diseases worldwide [17], being considered as a public health problem in children, culminating in excessive costs [18]. In this sense, interventions, highlighting probiotic supplementation, have been proposed in order to reduce the incidence of this disease. Recent studies indicate that

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probiotic supplementation reduces the risk of caries [17, 19], since they may play a role as antagonist agent on *Streptococcus mutans* and other acidogenic and aciduric microorganisms [17], being linked not only to the incidence reduction but also to the treatment of this disease [14, 18], although the literature concerning the effects of these microorganisms is still conflicting [20]. Nonetheless, whether probiotic supplementation is more efficient to replace conventional caries treatment remains to be elucidated. Thus, this review aimed at appraises trials assessing probiotics for managing caries and examine whether this intervention can replace conventional treatment in humans.

Methods

Eligibility criteria

In the present review, we only included trials assessing the in vivo role of probiotic supplementation on caries (incidence, risk factor, etc.) in subjects without any stated medical condition and published in the English language.

Search strategy

The search of the studies was carried out using the PubMed database in October 2017, without limiting the publication period. Keywords were selected from Mesh (Medical Subject Headings) and combined as "Probiotics" AND "Dental caries."

A total of 165 articles was found, including experimental studies with animals ($n = 4$), in vitro ($n = 41$), in situ ($n = 1$), review articles ($n = 64$), and human studies ($n = 55$). Regarding the human trials, 18 studies did not meet the inclusion criteria and two articles did not provide the complete version, resulting in 35 original articles included in this review. We also included seven trials that were not found in the search but were cited in the review articles evaluated. Finally, we included 42 original articles in the present study.

Probiotics vs caries: human studies over the years

Lactobacillus genus

Studies evaluating probiotics in caries were first developed in 2001. Näse et al. [14] observed that children presented lower caries incidence after consumption of milk containing *Lactobacillus rhamnosus* GG, compared with consumption of milk without probiotics. This research group also evaluated the effect of probiotics on caries prevention during 3 weeks. It was observed that the consumption of cheese supplemented with probiotics *Lactobacillus rhamnosus* GG ATCC 53103 and *Lactobacillus rhamnosus* LC 705 by young adults reduced by 20 and 27% the oral concentration of *Streptococcus mutans* and yeasts, respectively. This effect was observed only after, but not during the treatment, evidencing that the therapeutic effect occurs after probiotic colonization in the oral cavity [10].

Similar results were obtained by Glavina et al. [21] after administering yogurt containing *Lactobacillus rhamnosus* GG ATCC 53103 to children during 14 days. After 30 days of the intervention, there was a reduction in *Streptococcus mutans* count in saliva of the probiotic group, but no statistically significant difference in *Lactobacillus* count. Moreover, the study did not present the probiotic dose, which makes difficult data comparison.

Juneja and Kakade [22] supplemented *Lactobacillus rhamnosus* hct 70 for 3 weeks to children with medium and high caries activity, using milk as a vehicle. Saliva samples were collected three times: in the baseline period, immediately after intervention, and 3 weeks after the intervention. Probiotic supplementation reduced *Streptococcus mutans* count immediately after intervention and also after 3 weeks, where the effect was significantly more pronounced compared with baseline and placebo. Taking into account that children used non-fluoridated toothpaste and did not receive fluoride application or other dental treatments during the experimental period, the therapeutic effect observed was only due to probiotic supplementation. The consumption of milk also reduced *Streptococcus mutans*, indicating anticariogenic effect of this food [22].

Stecksén-Blicks et al. [23] administered *Lactobacillus rhamnosus* LB21 during 21 months, in combination with fluoride. A reduced incidence of caries was observed in the treated group; however, because there was no group supplemented with only probiotics (no fluoride), it is not possible to guarantee that the therapeutic effect is actually from *Lactobacillus rhamnosus* LB21. Differently, an elegant study in 2011 [24] evaluated the effect of milk containing probiotic and/or fluoride. Individuals were distributed into four groups: 1—receiving standard milk (placebo); 2—receiving milk containing *Lactobacillus rhamnosus* LB21 (10^7 CFU/mL) and fluoride; 3—receiving milk containing only *Lactobacillus rhamnosus* LB21 (10^7 CFU/mL); and 4—receiving milk containing only fluoride. All groups received 200 mL of milk per day for 15 months. In groups 2, 3, and 4, there were more cases of Root Caries Index (RCI) reversal, compared with placebo (group 1). There was also improvement of caries lesions in these groups. Concerning microbial counts, there was no difference between groups. Interestingly, therapeutic effects were more pronounced in groups receiving fluoride, especially group 2, that received both interventions, evidencing that probiotics can be used as adjuvants, but not replace fluoride treatment.

Recently, the probiotic *Lactobacillus rhamnosus* was tested again. It was observed that in the treated group, the prevalence (54.4% in the probiotic group and 65.8% in the placebo group) and the incidence of caries (9.7%

new cases in the probiotic group and 24.3% in the placebo group) were lower [12].

Contrary to the abovementioned studies, Montalto et al. [25] observed that oral supplementation with a pool of *Lactobacillus*, containing the strains *Lactobacillus sporogens*, *Lactobacillus bifidum*, *Lactobacillus bulgaricus*, *Lactobacillus termophilus*, *Lactobacillus acidophilus*, *Lactobacillus casei*, and *Lactobacillus rhamnosus*, in liquid form or capsule, increased the *Lactobacillus* oral count, but did not alter the *Streptococcus mutans* count. Based on these studies, it could be suggested that the probiotic with the main effect is *Lactobacillus rhamnosus*, and this effect was less pronounced in the study of Montalto et al. [25] as a result of the lower administered dose compared to the other studies. In addition to this probiotic, evidence suggests that *Lactobacillus casei* Shirota also played an important role in reducing *Streptococcus mutans* oral count in children [26].

Others studies involving more than one *Lactobacillus* did not find beneficial effects, reinforcing the theory that supplementation with only one probiotic may be better than mixing several microorganisms, even though belonging to the same genus [27–30], although some trials do not corroborate these results [31, 32].

Besides *Lactobacillus rhamnosus*, other species of *Lactobacillus* genus were tested. Chuang et al. [22] observed that *Lactobacillus paracasei* GMNL-33 reduced *Streptococcus mutans* count when administered in adults, during 2 weeks, showing a reduction in the risk of caries. Similar results were obtained when *Lactobacillus paracasei* SD1 was offered to children [33] and adults [34]. In addition to the reduction of *Streptococcus mutans* oral count, there was an increase in *Lactobacillus* oral count [34] and in the salivary concentrations of neutrophil peptide 1–3, an immunological marker that is reduced in caries-susceptible children [22, 33]. Supplementation with inactivated cells of *Lactobacillus paracasei* DSMZ16671 also reduced *Streptococcus mutans* oral count [35]; however, it is worth mentioning that inactivated cells are not considered as probiotics by the World Health Organization [1, 2].

An interesting study developed by Hasslöf et al. [36] showed that supplementation with *Lactobacillus paracasei* F19 (LF19) did not influence caries incidence when administered in babies (aged 4 to 13 months old) and evaluated at the age of 9 years old. It was also observed that the administered probiotic was not able to colonize the oral microbiota.

A similar trial was performed by Stensson et al. [37] that aimed to evaluate whether the supplementation with *Lactobacillus reuteri* strain ATCC 55730 for pregnant women during the last month of gestation and in the first year of life of the neonates (10^8 CFU/day) improved the oral health of these children at the age of nine. It was observed that 82% of the children from the probiotic group did not present caries. This value was much higher when compared to the placebo group (only 58% without caries). The prevalence of caries lesions and gingivitis were also lower in the probiotic group. In conclusion, the authors pointed out that probiotic supplementation in pregnancy and in the first year of life reduces caries incidence at the age of 9 years old. This same probiotic also reduced *Streptococcus mutans* oral count, after 3 weeks of supplementation, in young adults without topical fluoride treatment within 4 weeks prior to the study [38].

Cildir et al. [39] evaluated the effect of *Lactobacillus reuteri* strains DSM 17938 and ATCC PTA 5289 (1×10^8 CFU/day) in children (4–12 years) with cleft lip/palate during 25 days, but there was no statistically significant difference in the salivary count of *Streptococcus mutans* and *Lactobacillus* with the treatment. Equally, these strains did not profoundly affect caries lesions in adolescents, indicating that this probiotic may not have an important role in this disease [40].

Otherwise, Nishihara et al. [41] observed that supplementation with isolated *Lactobacillus salivarius* strains WB21 (6.7×10^8 CFU/day) and TI 2711 (2.8×10^8 CFU/day), for 2 weeks, decreased *Streptococcus mutans* count and increased *Lactobacillus* count in saliva of adults, improving oral health and reducing the caries risk. Recently, Sañudo et al. [42] observed that supplementation with inactivated cells of *Lactobacillus salivarius* CECT 5713 also reduced the oral count of *Streptococcus mutans*, but as previously mentioned, inactivated cells are not considered probiotics.

Lactobacillus brevis CD2 also reduced *Streptococcus mutans* oral count, plate acidogenicity, and bleeding when administered to high caries risk children for 6 weeks. Interestingly, children were instructed not to use products containing fluoride and, therefore, we could infer that the anticariogenic effect was only due to probiotic supplementation [43].

Bifidobacterium genus

As mentioned above, several studies suggested the effect of lactobacilli-derived probiotics in affecting oral ecology and reducing caries risk factors and incidence. Nevertheless, the effect of bifidobacteria supplementation was only reported in few studies. In 2005, Caglar et al. [44] observed a reduction of *Streptococcus mutans* oral count after short consumption (2 weeks) of yogurt containing *Bifidobacterium* DN-173 010 in young adults that did not use fluoride within 4 weeks prior to the study. Similar results were obtained with *Bifidobacterium animalis* subsp. *lactis* BB-12 supplementation to adults, during 10 days, using ice cream as the food matrix [30]. However, further studies did not confirm the anticariogenic effect of bifidobacteria.

Taipale et al. [45] administered *Bifidobacterium animalis* subsp. *lactis* BB-12 for babies (1–2 months), during 14.9 ± 6.7 months, and observed that probiotic supplementation did not affect the oral count of *Streptococcus mutans*, *Lactobacillus*, and yeasts at the ages of 8 months and 2 years [46]. Moreover, there was no difference in caries incidence of these children at the age of 4 years, indicating that *Bifidobacterium animalis* subsp. *lactis* BB-12 administration in the early childhood does not reduce the risk of caries [45]. Other trials also failed in demonstrating therapeutic effects of this probiotic and other species of *Bifidobacterium* genus on dental caries in patients with no use of fluoride [47, 48].

Interestingly, Nozari et al. [48] observed that traditional yogurt ingestion, but not yogurt containing *Bifidobacterium lactis*, reduced *Streptococcus mutans* and *Lactobacillus* oral count in children. Dairy products are considered food that prevents caries because they are sources of minerals, especially calcium [1, 2]. In this context, the food matrix may also have a therapeutic effect and, in some studies, it may be questionable whether the therapeutic effect is derived from the matrix or the probiotic.

Streptococcus genus

In 2009, a pilot study with 20 individuals tested the efficacy of a mouthwash containing *Streptococcus oralis* strain KJ3sm, *Streptococcus uberis* strain KJ2sm, and *Streptococcus rattus* strain JH145, in two doses, 10^6 or 10^8 CFU of each probiotic, during 4 weeks. The group treated with the higher dose showed a decrease in salivary *Streptococcus mutans* count, by 60%, compared with the baseline level. Moreover, there was a reduction of the pathogens *Campylobacter rectus* and *Porphyromonas gingivalis* in the subgingival plaque in the same group, although there was no statistically significant difference [49].

Burton et al. [22, 50] observed that *Streptococcus salivarius* strain M18 administration during 3 months increased its oral count, as well as reduced the *Streptococcus mutans* count in children with caries. Moreover, there was a reduction of bacterial plaque scores in the treated individuals, evidencing an improvement in oral health. None of the supplemented individuals had adverse effects, indicating the safety of this treatment. In other studies, the association of microorganisms from *Streptococcus* genus (*Streptococcus uberis* KJ2, *Streptococcus oralis KJ3*, and *Streptococcus rattus* JH145), in the probiotic group ProBiora3, reduced the risk of the development of caries [18, 51].

Combination or comparison between different genres

Singh et al. [52] supplemented children with ice cream containing probiotics (*Bifidobacterium lactis* Bb-12 ATCC27536 and *Lactobacillus acidophilus* La-5) or placebo during 10 days. The probiotic group presented lower *Streptococcus mutans* count in saliva compared with baseline, but there was no difference in *Lactobacillus* levels. In placebo group (ice cream without probiotic), there was also a reduction in *Streptococcus mutans* oral count; however, there was no statistically significant difference. This data highlighted that the dairy foods may also have a therapeutic effect. There was no statistically significant difference between probiotic and placebo groups. A similar trial also observed that these probiotics reduced *Streptococcus mutans* oral count in children; however, after 6 months of the intervention, *Streptococcus mutans* oral concentrations returned to the baseline values, evidencing that probiotic supplementation should be continuous to maintain the therapeutic effects [53]. Another studies supplementing species from *Bifidobacterium* and *Lactobacillus* genres also observed a reduction in *Streptococcus mutans* oral count [54, 55], even in individuals with no use of fluoride treatments [55].

Yousuf et al. [56] investigated whether there was a synergism between *Bifidobacterium* and *Lactobacillus* genres. They supplemented schoolchildren with *Lactobacillus acidophilus*, *Bifidobacterium longum*, *Bifidobacterium bifidum*, and *Bifidobacterium lactis* (group A); only with *Lactobacillus acidophilus* (group B); or with placebo (group C) during 3 weeks and observed a reduction of *Streptococcus mutans* oral count in groups A and B. Possibly, *Lactobacillus acidophilus* presents the main anticariogenic effect and there was no synergism between these probiotics.

In 2013, Cannon et al. [57] supplemented medium- to high-caries-risk children with *Lactobacilli reuteri* for 28 days (group A) or with *Streptococcus uberis* KJ2, *Streptococcus oralis* KJ3, and *Streptococcus rattus* JH145 during 30 days (group B). After interventions, both groups presented lower levels of *Streptococcus mutans* in saliva, indicating a reduction of caries risk. There was also reduction of *Lactobacillus* in saliva after interventions, but the authors did not discuss this result.

Table 1 summarizes the results from the abovementioned studies.

Main results

The therapeutic effects of *Lactobacillus* genus are better elucidated in the literature when compared with other genres (*Bifidobacterium* and *Streptococcus*). Among the main effects presented by this genus, we highlight:

1. Reduction of *Streptococcus mutans* oral count;
2. Increase in *Lactobacillus* oral count;
3. Reduction in caries incidence.

Concerning the *Bifidobacterium* supplementation, the results are conflicting but most of the trials did not observe anticariogenic role of these probiotics. Only a few

Table 1 Studies involving probiotic supplementation in caries risk factors and incidence in humans (chronological order)

Number of participants	Age	Probiotic and amount	Treatment duration	Probiotic effect	Reference
594	1–6 years	*Lactobacillus rhamnosus* GG ATCC (LGG) 53103 5–10 × 10^5 CFU/mL	7 months	Reduction in the caries incidence.	[14]
74	18–35 years	*Lactobacillus rhamnosus* GG ATCC 53103 1.9 × 10^7 CFU/g *Lactobacillus rhamnosus* LC 705 1.2 × 10^7 CFU/g	3 weeks	Tendency of *Streptococcus mutans* reduction in the oral cavity, but without statistical difference.	[10]
261	2–3 years	*Lactobacillus rhamnosus* SP1 10^7 CFU/mL	10 months	Reduction of caries prevalence (54.4% in the probiotic group and 65.8% in the placebo group) and incidence (9.7% new cases in the probiotic group and 24.3% in the placebo group).	[13]
35	–	1.88 × 10^9 live cells/day: *L. sporogens* 16%, *L. bifidum* 12%, *L. bulgaricus* 12%, *L. termophilus* 18%, *L. acidophilus* 20%, *L. casei* 10%, *L. rhamnosus* 12%	45 days	Increase *Lactobacilli* count but not reduce *Streptococcus mutans* count.	[25]
21	21–24 years	*Bifidobacterium* DN-173 010 7 × 10^7 CFU/g	2 weeks	Reduction of *Streptococcus mutans* oral count.	[44]
120	21–24 years	*Lactobacillus reuteri* ATCC 55730 10^8 CFU	3 weeks	Reduction of *Streptococcus mutans* oral count.	[38]
80	21 - 24 years	*Lactobacillus reuteri* DSM 17938 and ATCC PTA 5289 1.1 × 10^8 CFU of each strain	3 weeks	Reduction of *Streptococcus mutans* oral count.	[31]
20	Mean age 20 years	*Lactobacillus reuteri* DSM 17938 and ATCC PTA 5289 1 × 10^8 CFU of each strain	10 days	Reduction of *Streptococcus mutans* oral count.	[32]
24	Mean age 20 years	*Bifidobacterium lactis* Bb-12 1 × 10^7 CFU/g–53 g/day	10 days	Reduction of *Streptococcus mutans* count.	[30]
248	1–5 years	*Lactobacillus rhamnosus* LB21 10^7 CFU/ml–150 ml per day	21 months	Reduction in the caries incidence.	[23]
20	21–35 years	*Streptococcus oralis* strain KJ3sm, *Streptococcus uberis* strain KJ2sm and *Streptococcus rattus* strain JH145, in two doses, 10^6 or 10^8 CFU of each probiotic per day	4 weeks	Reduction of *Streptococcus mutans* count.	[49]
78	20–26 years	*Lactobacillus paracasei* GMNL-33	2 weeks	Reduction of *Streptococcus mutans* count.	[11]
100	58–84 years	*Lactobacillus rhamnosus* LB21 10^7 CFU/mL	15 months	RCI reversal and improvement of caries lesions.	[24]
40	12–14 years	*Bifidobacterium lactis* Bb-12 ATCC27536 and *Lactobacillus acidophilus* La-5 1 × 10^6 CFU/g of each strain	10 days	Reduction of *Streptococcus mutans* count, but not in *Lactobacillus* levels in saliva.	[52]
13	Mean age 25.3 years	*Lactobacillus rhamnosus* GG and *Lactobacillus reuteri*	2 weeks	No effect.	[27]
30	Mean age 26 years	*Lactobacillus reuteri* DSM 17938 and ATCC PTA 5289 1 × 10^8 CFU of each strain	2 weeks	No effect.	[28]
62	Mean age 23 years	*Lactobacillus reuteri* DSM 17938 and ATCC PTA 5289 1 × 10^8 CFU of each strain	6 weeks	No effect.	[29]
106	1–2 months	*Bifidobacterium animalis* subsp. *lactis* BB-12 (BB-12) 10^{10} CFU/day	14.9 ± 6.7 months	*Lactobacillus* oral count. No effect.	[46]

Table 1 Studies involving probiotic supplementation in caries risk factors and incidence in humans (chronological order) *(Continued)*

Number of participants	Age	Probiotic and amount	Treatment duration	Probiotic effect	Reference
40	12–15 years	*Lactobacillus rhamnosus* hct 70 2.34×10^9 CFU/day	3 weeks	Reduction of *Streptococcus mutans* count in saliva.	[22]
25	6–10 years	*Lactobacillus rhamnosus* GG ATCC 53103	14 days	Reduction of *Streptococcus mutans* count in saliva.	[21]
19	4–12 years	*Lactobacillus reuteri* strains DSM 17938 and ATCC PTA 5289 1×10^8 CFU/day	25 days	No effect.	[39]
191	6–8 years	*Lactobacillus brevis* CD2 2×10^9 colonies	6 weeks	Reduction of *Streptococcus mutans* oral count, plate acidogenicity and bleeding.	[43]
26	–	*Bifidobacterium animalis* subsp. *lactis*DN-173010	2 weeks	No effect.	[47]
20	–	*Lactobacillus paracasei* DSMZ16671	2 days	Reduction of *Streptococcus mutans* oral count.	[35]
40	18–25 years	*Lactobacillus paracasei* SD1 $7.5 \pm 0.20 \times 10^8$ CFU/g	4 weeks	Reduction of *Streptococcus mutans* and increase in	[34]
179	4 months	*Lactobacillus paracasei* F19 (LF19) 1×10^8 CFU/day	9 months	No effect.	[36]
100	5–10 years	*Streptococcus salivarius* strain M18 3.66×10^9 CFU/day	3 months	Increase in *Streptococcus salivarius* count, reduction of *Streptococcus mutans* count and in the plaque score.	[50]
60	6–12 years	*Lactobacilli reuteri* (2×10^8 CFU/day) or *S. uberis* KJ2, *S. oralis* KJ3, and *S. rattus* JH145 ($\geq 1 \times 10^8$ CFU/day)	28–30 days	Reduction of *Streptococcus mutans* and *Lactobacillus* in saliva.	[57]
106	1–2 months	*Bifidobacterium animalis* subsp. *lactis* BB-12 (BB-12) 10^{10} CFU/day	14.9 ± 6.7 months	No effect.	[45]
64	Mean age 24.8 ± 2.3 years	*Lactobacillus salivarius* strains WB21 (6.7×10^8 CFU/day) and TI 2711 (2.8×10^8 CFU/day)	2 weeks	Reduction of *Streptococcus mutans* and increase of *Lactobacillus* in saliva.	[41]
113	Last month of pregnancy and first year of life	*Lactobacillus reuteri* 10^8 CFU/day (mothers and children)	13 months	Reduction of caries incidence.	[37]
31	6–8 years	*Lactobacillus casei* Shirota	10 days	Reduction of *Streptococcus mutans* oral count.	[26]
36	12–17 years	*Lactobacillus reuteri* (DSM 17938 and ATCC PTA 5289) 1×10^8 CFU of each strain/day	3 months	Tendency of less demineralization on early enamel lesions, but without significant difference.	[40]
60	–	*Lactobacillus paracasei* SD1 $7.5 \pm 0.20 \times 10^8$ CFU/g	6 months	Reduction of *Streptococcus mutans* and increase in neutrophil peptide 1–3 oral count.	[33]
50	6–12 years	*Bifidobacterium lactis* Bb-12 and *Lactobacillus acidophilus* La-5 (1×10^6 CFU of each) or *Lactobacillus casei* strain Shirota (6.5×10^9)	7 days	Reduction of *Streptococcus mutans* oral count.	[54]
60	6–12 years	*Bifidobacterium lactis* Bb-12 and *Lactobacillus acidophilus La-5* 1×10^6 CFU of each probiotic	7 days	Reduction of *Streptococcus mutans* oral count.	[53]
49	6–12 years	*Bifidobacterium lactis* 1×10^6 CFU/g	2 weeks	No effect.	[48]
40	4–6 years	*Streptococcus uberis* KJ2, *S. oralis KJ3*, and *S. rattus* JH145	2 weeks	Reduction of *Streptococcus mutans* oral count.	[51]
33	12–15 years		3 weeks		[56]

Table 1 Studies involving probiotic supplementation in caries risk factors and incidence in humans (chronological order) *(Continued)*

Number of participants	Age	Probiotic and amount	Treatment duration	Probiotic effect	Reference
		Lactobacillus acidophilus, *Bifidobacterium longum*, *Bifidobacterium bifidum*, and *Bifidobacterium lactis*		Reduction of *Streptococcus mutans* oral count.	
138	2–3 years	*Streptococcus uberis* KJ2, *S. oralis KJ3*, and *S. rattus* JH145 1×10^8	1 year	Reduction of the risk of developing caries.	[18]
11	23–44 years	*Lactobacillus salivarius* CECT 5713 10^9 inactivated cells per day	1 week	Reduction of *Streptococcus mutans* oral count.	[42]
50	19–27 years	*Lactobacillus acidophilus* ATCC 4356 and *Bifidobacterium bifidum* ATCC 29521 1.5×10^8 CFU/g	3 weeks	Reduction of *Streptococcus mutans* oral count.	[55]

studies evaluated the effects of *Streptococcus* genus; although they presented positive effects, the data in the literature are scarce to recommend the use of these microorganisms. Some trials evaluated the effect of more than one probiotic; however, evidence suggested no synergism between microorganisms, especially regarding *Lactobacillus* genus.

Conclusions

Proper tooth hygiene, fluoride, and reduced consumption of sugary foods are considered effective methods to prevent and treat caries. Of these, fluoride would be the only treatment that could be replaced by probiotic supplementation. However, in several of the studies presented, there is no exclusion of this treatment. In addition, in most studies, it is not mentioned whether fluoride treatment was being applied. Only a few studies evaluated probiotics without fluoride. While some of them presented therapeutic effect of isolated probiotics, one trial showed better effects when both interventions were applied together, indicating that probiotics can be used as adjuvants in caries treatment, but are not able to replace the conventional therapy. In any case, the number of studies is scarce to recommend supplementation with probiotics as the main treatment for dental caries.

Abbreviations

CFU: Colony-forming unit; Mesh: Medical Subject Headings; RCI: Root Caries Index

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

The search of the studies and the initial manuscript preparation were performed by AYC, AB, and RR and revised by JT. The final manuscript version was revised by MMR. All authors agreed on the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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