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Meta-analyses

Meta-analysis of randomized controlled trials of the effects of probiotics on functional constipation in adults

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Summary

Background & aims

Clinical trials have reported controversial results regarding the effectiveness of probiotics in alleviating functional constipation in adults. We reviewed relevant randomized controlled trials to elucidate the effectiveness of probiotics on constipation symptoms in adults with functional constipation.

Methods

We searched Medline, the Cochrane Library, Web of Science, and Google Scholar for relevant articles published up to April 2019. The primary outcomes of interest were stool frequency, gut transit time (GTT), stool consistency, and bloating. Two authors independently performed the study selection, risk-of-bias assessment, and data extraction. The outcome data were extracted from each included study and synthesized using weighted mean differences (WMDs) or standardized mean differences (SMDs). Pooled data synthesis was performed using a random-effects model.

Results

In total, 2327 relevant studies were identified, 15 of which were found to be eligible randomized controlled trials and were included in the meta-analysis. Pooling of the extracted data demonstrated that probiotic consumption significantly reduced the whole GTT by 13.75h [95% confidence interval (CI): −21.93 to −5.56h] and increased the stool frequency by 0.98 (95% CI: 0.36 to 1.60) bowel movements per week. This increase

was significant with the consumption of multispecies probiotics [at least two bacteria; WMD: 1.22 (95% CI: 0.50 to 1.94) bowel movements per week] but not with the consumption of *Bifidobacterium lactis* [WMD: 1.34 (95% CI: -0.27 to 2.94) bowel movements per week] or *B. longum* [WMD: -0.02 (95% CI: -0.56 to 0.53) bowel movements per week] alone. Multispecies probiotics (WMD: 1.37; 95% CI: 0.72 to 2.01), but not single-species probiotics (WMD: 1.18; 95% CI: -0.59 to 2.96), improved stool consistency (WMD: 1.30; 95% CI: 0.22 to 2.38). Similarly, multispecies probiotics (at least two bacteria; WMD: -0.49; 95% CI: -0.85 to -0.13), but not single-species probiotics (WMD: -0.24; 95% CI: -0.55 to 0.07), significantly decreased bloating. Performance bias were high, whereas detection bias was unclear because of inadequate reporting.

Conclusion

Consumption of probiotics, in particular, multispecies probiotics, may substantially reduce the GTT, increase the stool frequency, and improve the stool consistency. Thus, probiotics can be regarded as safe and natural agents for alleviation of functional constipation in adults.

Introduction

Constipation is one of the most common functional gut disorders worldwide, with a prevalence of 5%–20%, and is characterized by a low defecation frequency, prolonged gastrointestinal tract emptying time, or predominantly, incomplete defecation [[1], [2], [3]]. In addition to its adverse effects on quality of life, constipation comes with economic burden for a person seeking treatment. The direct cost of constipation ranged from \$1912 to \$7522 per year per patient [4,5]. However, the treatment of functional constipation is challenging. Osmotic and stimulant laxatives, stool softeners, bulking agents, and secretagogues are commonly used to treat constipation; however, approximately half of patients are dissatisfied with these treatment strategies because of their limited efficacy [6,7]. Probiotics are “live microorganisms that, when administered in adequate amounts, confer a health benefit on the host” [8]. Over the past decade, numbers of studies have evaluated the effectiveness of probiotics in alleviating functional constipation and have suggested that their effect is mediated by the regulation of aberrant gut motility via action on the intestinal microbiota, leading to the production of metabolites such as tryptamine [9] and short-chain fatty acids [10] that interact with the host immune system and enteric nervous system.

One meta-analysis reported that probiotics may improve stool frequency, gut transit time (GTT), and stool consistency, and their subgroup analysis based on probiotic species revealed *Bifidobacterium lactis* as the most beneficial probiotic [11]. However, although some studies have reported favorable results for probiotics, their clinical efficacy in alleviating constipation remains controversial because of small sample sizes, high heterogeneity, and high risks of bias in the individual studies and limitations of their analysis methods. Furthermore, some recently published randomized controlled trials (RCTs) on this topic have also reported conflicting results [[12], [13], [14], [15], [16]]. Another meta-analysis only investigated the effects of probiotics on stool frequency and intestinal transit in constipation adults [17], besides some meta-analysis only reported the effects of probiotics in the treatment of functional constipation in children [[18], [19], [20]] or elderly people [21]. Our meta-analysis focused on adults (≥ 18 years) with constipation and various clinical indicators of constipation, such as stool frequency, GTT, stool frequency and bloating.

The aim of this meta-analysis was to broadly evaluate the latest (up to April 2019) studies on the clinical outcomes of probiotic supplementation in adults with constipation and to determine the probiotic species

or strains, number of probiotic species, probiotic dose, and duration of probiotic supplementation that are most effective in treating functional constipation in adults.

Section snippets

Search strategy

This meta-analysis was conducted and reported in accordance with the guidelines of the Cochrane Handbook [22] and the relevant criteria of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [23]. A systematic search of published studies was performed using the Cochrane Central Register of Controlled Trials (<http://onlinelibrary.wiley.com/cochranelibrary/search/>; up to April 2019), Medline (<http://www.ncbi.nlm.nih.gov/pubmed/>; up to April 2019), Web of...

Included studies and their characteristics

Figure 1 presents the PRISMA flowchart that describes the study selection process and the reasons for exclusion of studies. In total, 2327 related articles were identified by searching the electronic databases. After eliminating duplicate studies, the remaining 1912 studies were screened by title/abstract, 1861 of which were eliminated as they did not fulfill the inclusion criteria. The remaining 51 studies were screened by full text, 15 qualitative studies of which met the eligibility criteria ...

Discussion

A number of meta-analysis studies suggested that probiotics administration have protective effects against a range of dysfunctions such as cardiovascular disease [43], age-related diseases [44] and intestinal diseases [45]. Clinical trials have reported controversial results regarding the effectiveness of probiotics in alleviating functional constipation in adults [12]. Compared to previous published meta-analysis studies [11,17,18,20,21, [46], [47], [48], [49]], our analysis specifically...

Limitations

This meta-analysis has some limitations. First, most of the included studies had relatively modest sample sizes, which may have caused overestimation of the intervention effect; therefore, large-scale trials are warranted. Second, some analyzed studies did not report sufficient information about sequence generation, adherence of patients to treatment, and outcomes. The probiotic characteristics (e.g., isolation sources, doses, and duration of treatment) and participant characteristics (e.g.,...

Conclusion

In summary, probiotic supplementation can improve stool frequency, GTT, and stool consistency in adults with functional constipation. Notably, multispecies probiotic supplements are more beneficial than single-species supplements. Future clinical studies with a superior study design and a large sample size that

consider confounders that influence the gut microbial composition and the participant characteristics (baseline gut microbiota, country of origin, age, and other lifestyle factors), are...

Conflict of interest

The authors declare that they have no competing interests....

Acknowledgment

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[Perspective: fundamental limitations of the randomized controlled trial method in nutritional research: the example of probiotics](#)

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F. Hendijani *et al.*

[Probiotic supplementation for management of cardiovascular risk factors in adults with type II diabetes: a systematic review and meta-analysis](#)

Clin Nutr (2018)

K. Matsumoto *et al.*

[Effects of a probiotic fermented milk beverage containing Lactobacillus casei strain Shirota on defecation frequency, intestinal microbiota, and the intestinal environment of healthy individuals with soft stools](#)

J Biosci Bioeng (2010)

A. Ishizuka *et al.*

[Effects of administration of Bifidobacterium animalis subsp. lactis GCL2505 on defecation frequency and bifidobacterial microbiota composition in humans](#)

J Biosci Bioeng (2012)

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[Effects of probiotics on D-galactose-induced oxidative stress in plasma: a meta-analysis of animal models](#)

J Funct Foods (2017)

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Influence of consumption of probiotics on the plasma lipid profile: a meta-analysis of randomised controlled trials

Nutr Metab Cardiovasc Dis (2011)

S. Jayasimhan *et al.*

Efficacy of microbial cell preparation in improving chronic constipation: a randomized, double-blind, placebo-controlled trial

Clin Nutr (2013)

M.I. Martínez-Martínez *et al.*

The effect of probiotics as a treatment for constipation in elderly people: a systematic review

Arch Gerontol Geriatr (2017)

A. Wegner *et al.*

The effectiveness of *Lactobacillus reuteri* DSM 17938 as an adjunct to macrogol in the treatment of functional constipation in children. A randomized, double-blind, placebo-controlled, multicentre trial

Clin Res Hepatol Gastroenterol (2018)

E. Dimidi *et al.*

The effect of probiotics on functional constipation in adults: a systematic review and meta-analysis of randomized controlled trials

Am J Clin Nutr (2014)



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Evaluating the effectiveness of probiotics in relieving constipation in Parkinson's disease: A systematic review and meta-analysis

2023, Heliyon

Show abstract

A randomized controlled trial of an oral probiotic to reduce antepartum group B *Streptococcus* colonization and gastrointestinal symptoms

2023, American Journal of Obstetrics and Gynecology MFM

Citation Excerpt :

...The management of GI symptoms of pregnancy presents challenges for pregnant people and providers.³¹ Multispecies probiotic interventions have been shown to significantly increase gut transit time and stool frequency and enhance consistency in constipated (nonpregnant) adults.³² Probiotic group participants had reduced GI symptoms of pregnancy after 8 weeks of the intervention....

[Show abstract](#) 

Probiotics and synbiotics in chronic constipation in adults: A systematic review and meta-analysis of randomized controlled trials

2022, Clinical Nutrition

Citation Excerpt :

...Regarding probiotics, the first systematic review and meta-analysis in 2014 identified 14 randomized controlled trials (RCTs) and reported a beneficial effect of *Bifidobacterium lactis* on stool frequency and consistency, but not *Lactobacillus casei* Shirota [13]. A subsequent systematic review of 15 RCTs found no effect of *B. lactis* on stool frequency, whereas multispecies probiotics improved constipation outcomes [14]. The evidence for synbiotics in chronic constipation is sparse, with a systematic review in 2014 identifying only two RCTs and demonstrating efficacy on response to therapy [15]....

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Comparative study on alleviating effect of kiwi berry (*Actinidia arguta*) polysaccharide and polyphenol extracts on constipated mice

2022, Food Research International

Citation Excerpt :

...Studies have shown that Rk3 supplementation changed the negative effect of intaking antibiotic, increased Bacteroidetes levels, and reduced Firmicutes/Bacteroidetes ratios to levels like those of normal mice (Ohkusa, Koido, Nishikawa, & Sato, 2019). Lactulose restored intestinal bacterial diversity and reconstructed intestinal bacterial community in constipation mice by reducing the ratio of Firmicutes/Bacteroides (Zhang et al., 2020). The results of this study show that feeding kiwi berry polysaccharide and polyphenol extracts to constipated mice resulted in a lower Firmicutes level but higher Bacteroidetes level of both colon and fecal microbial communities....

[Show abstract](#) 

Fecal bacterial microbiota in constipated patients before and after eight weeks of daily *Bifidobacterium infantis* 35624 administration

2022, Revista de Gastroenterologia de Mexico

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Characteristics of fecal microbiota in different constipation subtypes and association with colon physiology, lifestyle factors, and psychological status

2023, Therapeutic Advances in Gastroenterology

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Research article

Efficacy of pasteurised yoghurt in improving chronic constipation: A randomised, double-blind, placebo-controlled trial

International Dairy Journal, Volume 40, 2015, pp. 1-5

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Research article

Gut microbiota alterations from different *Lactobacillus* probiotic-fermented yoghurt treatments in slow-transit constipation

Journal of Functional Foods, Volume 38, Part A, 2017, pp. 110-118

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Research article

Mechanisms, Evaluation, and Management of Chronic Constipation

Gastroenterology, Volume 158, Issue 5, 2020, pp. 1232-1249.e3

[Show abstract](#) ✓

Research article

Laxative effect of probiotic chocolate on loperamide-induced constipation in rats

Food Research International, Volume 116, 2019, pp. 1173-1182

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Research article

Lactobacillus casei rhamnosus Lcr35 in the Management of Functional Constipation in Children: A Randomized Trial

The Journal of Pediatrics, Volume 184, 2017, pp. 101-105.e1

[Show abstract](#) ✓

Research article

Differential structures and enterotype-like clusters of *Bifidobacterium* responses to probiotic fermented milk consumption across subjects using a *Bifidobacterium*-target procedure

Food Research International, Volume 140, 2021, Article 109839

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