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RESEARCH & PRACTICE
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Probiotics in the management of lower gastrointestinal symptoms



Prof. Giovanni Barbara

Giovanni Barbara is Professor of Internal Medicine and Gastroenterology at the Department of Digestive Diseases and Internal Medicine of the University of Bologna, Italy. He has published extensively in the field of functional gastrointestinal disorders, infectious disease, inflammatory bowel disease, and microbiota, and is member of the Editorial Board of several journals in the gastroenterology field. At present he is also President of the European Society of Neurogastroenterology and Motility (ESNM) as well as member of the Board of Directors of the Rome Foundation.

The burden of gastrointestinal symptoms

At present, gastrointestinal (GI) symptoms and digestive disorders account for one in ten consultations in primary care. According to the World Health Organization (WHO), the worldwide prevalence of irritable bowel syndrome (IBS—a functional gastrointestinal disorder) is around 11.2%. And furthermore, symptoms may affect generally healthy people: gut-related symptoms like bloating, heartburn, nausea, vomiting, constipation, diarrhea, flatulence, food intolerance, incontinence, and abdominal pain cause difficulties for up to one third of the global population. When experienced on a chronic basis, these symptoms can significantly affect quality of life.

A role for probiotics?

The therapeutic options are limited when it comes to functional gastrointestinal disorders; pharmacological treatments may have limited efficacy

and often come with side effects. However, given that changes in the gut microbiota have been implicated in the pathogenesis of some gastrointestinal disorders such as IBS, interest is growing in finding interventions that target the gut microbiota for improvement of symptoms. Probiotics are foremost among these therapies—so can they be employed to help manage lower gastrointestinal symptoms?

This “best of probiotics” document describes the latest evidence in this regard. What follows is a selection of articles published on the Gut Microbiota for Health website—collectively showing that probiotics can be a useful addition to the physician’s toolbox as a way of helping patients address a number of lower gastrointestinal symptoms.

This document also covers the notion that probiotics could have a preventative role to play: the articles that follow show the evidence for

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probiotics in both reducing inappropriate antibiotic prescriptions and preventing *Clostridium difficile* infection in hospitalized adults. They appear to be a low risk intervention, with a favourable safety profile reported in the literature.

Included in this document, notably, is an article covering the recent update by European Society for Primary Care Gastroenterology (member of United European Gastroenterology) of their practical reference guide on probiotics; this guide supports clinical decision-making about which probiotic to consider for managing specific lower GI symptoms in adults and in preventing diarrhea in patients receiving antibiotic therapy or *H. pylori* eradication therapy.

Looking toward the future

Alongside the necessity for more human research that elucidates the ideal uses of probiotics in clinical practice, a need for more education exists. Both physicians and patients benefit from knowledge on the strains, doses, and formulations that are supported by evidence at present.

The Gut Microbiota for Health website, an initiative of the ESNM's Gut Microbiota & Health section, has been instrumental in bringing about greater awareness about gut microbiota in health. The goals of this section are:

- To expand knowledge and interest in the field of neurogastroenterology and motility & educate a young generation of physicians on the basic and clinical science pertaining to the field
- To promote public scientific education on this topic
- To encourage basic and clinical research in neurogastroenterology and motility
- To establish standards for good clinical practice and patient care in this area

Gut Microbiota for Health is now celebrating 5 years—and with more than 50,000 engaged community members all over the globe, it continues to grow by sharing science-based messages about gut microbiota. We hope you enjoy this document and the ongoing efforts of the Gut Microbiota for Health team to champion information relevant to clinical practice.

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The contributions of gut microbiota and probiotics to gut motility and constipation

Published on July, 27, 2017 by Andreu Prados.



Andreu Prados holds a Bachelor of Science Degree in Pharmacy & Human Nutrition and Dietetics. Science writer specialised in gut microbiota and probiotics, working also as lecturer and consultant in nutrition and healthcare.

Constipation is a common condition that may result from altered gastrointestinal motility. Several factors appear relevant to gut motility: the gut luminal environment (including the gastrointestinal microbiota and fermentation), as well as factors related to the immune system, the enteric nervous system, and the central nervous system.

Previous research has found associations between colonic transit time and aspects of patients' gut microbiota in terms of composition, diversity, and also metabolic products. For instance, a longer colonic transit time was recently correlated with high microbial richness and with higher urinary levels of potentially harmful metabolites. In this line, a recent study, led by Dr. Jean-François Brugère from the Université d'Auvergne in France, explored the extent to which transit time could affect gut microbiota composition and metabolism, using a multi-compartmental *in vitro* continuous culture system simulating the physiological conditions of the proximal, transversal, and distal parts of the colon. The researchers found that an increase in transit time (96-hour transit time versus a normal 48 to 72-hour transit time) led to a decrease of both biomass and gut microbiota diversity in the

transversal and distal compartments of the system.

Specifically, increased transit time led to the decrease of sulfate-reducing bacteria, major competitors of methanogenic archaea. The subsequent increased levels of methane could mediate slower transit time, as a previous study showed that methane slows intestinal transit and augments small intestinal contractile activity. Besides this, increased transit time resulted in increased carbohydrate fermentation in the proximal compartments, whereas there was an increase of putrefaction activity in the compartments simulating the transversal and distal colon. As this *in vitro* system allowed to study of the effect of transit time as a single variable, it can be concluded that colonic transit time, independently of other factors, may affect both the composition and metabolic activity of the gut microbiota.

Colonic transit time, independently of other factors, may affect both the composition and metabolic activity of the gut microbiota

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The contributions of gut microbiota and probiotics to gut motility and constipation

There has been increasing evidence investigating the role of gut microbiota and possible microbiota-based therapies on gut motility and constipation. According to a recent review, the most explored microbiota-based therapies for constipation include dietary fibres, prebiotics, probiotics and faecal microbiota transplantation:

Dietary fibres

Fibres from plant foods (mainly vegetables, legumes, and fruits) can promote the excretion of bacterial fermentation products that can increase stool bulk and have pro-motility effects. Beyond a low-fibre diet, other factors may explain dysbiosis in chronic constipation. A recent observational study of 79 children aged 6 to 36 months (39 constipated children and 40 non-constipated children) found that constipated children had a smaller concentration of *Lactobacilli* in their stool than non-constipated children. Besides this, constipated children consumed more dairy products, were more frequently delivered via caesarean section, were weaned earlier and had a family history of constipation.

Prebiotics

Randomized controlled trials assessing the effect of prebiotics for the management of chronic constipation in both animals and humans have reported contradictory results and, thus, the effectiveness of prebiotics



in managing constipation in clinical practice remains unclear.

Probiotics

A recent systematic review and meta-analysis of 14 randomized controlled trials (n = 1182 participants) showed that administration of 10^8 to 3×10^{10} colony forming units (CFU)/day for 2 to 8 weeks of specific probiotic species and strains decreased gut transit time by 12 hours, increased stool frequency by 1.5 stools/week, and improved some constipation-related symptoms in adults with functional constipation. The probiotics were provided in yogurt, fermented milks, beverages, sachets, capsules, or probiotic-fortified foods. The effects of probiotics were species- and strain-specific, with different *Bifidobacterium lactis* strains improving gut transit time, stool frequency and consistency, and

flatulence, whereas the strain *Lactobacillus casei* Shirota did not confer any beneficial results.

Chronic constipation is a common problem among elderly people and a recent systematic review of 4 randomised and placebo-controlled trials suggests that administration of probiotics could be an alternative to traditional drug treatments in older individuals, as they significantly improved constipation by 10-40% compared to placebo controls without a probiotic. Studied probiotics included *Bifidobacterium longum*, *B. lactis*, and a mixture of *Lactobacillus*, *Bifidobacterium* and *Streptococcus* strains with doses from 10^9 to 4.5×10^{11} CFU/day for 6 to 25 weeks.

When considering constipation in adults with chronic disease, a recent randomized, double-blind, placebo-

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controlled trial found that the consumption of a fermented milk containing multiple probiotic strains and prebiotic fibre is superior to placebo in improving constipation in patients with Parkinson's disease.

Among the mechanisms involved in the effect of probiotics on gut motility and constipation, a recent review has proposed: (1) modification of the altered intestinal microbiota in patients with constipation ("microbiota-dependent" effect); (2) modulation of gut sensation and motility function through probiotic metabolites; (3) modification of the

intraluminal environment through increasing the end products of bacterial fermentation (e.g. saccharolytic bacteria, such as *Bifidobacterium* and *Lactobacillus* ferment fibres into short-chain fatty acids, which reduce intestinal pH and consequently increase intestinal motility), and (4) modulation of the mucosal immune barrier and/or systemic immune barrier and gut mucosal inflammation and altered sensory and motor functions. However, the contribution of each mechanism of probiotics on gut transit time and constipation is not fully understood and deserves further research.

Faecal microbiota transplantation (FMT)

There are few published studies assessing the efficacy of FMT on constipation but it is too early to make clear conclusions for its clinical use in constipation.

On the whole, the altered gut microbiota may play a role in the pathogenesis of chronic constipation. Although the exact mechanisms are poorly understood, microbiota-based therapies –specifically probiotics– are emerging as a promising tool for the management of chronic constipation.



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Read the original post online at:

<http://www.gutmicrobiotaforhealth.com/en/contributions-gut-microbiota-probiotics-gut-motility-constipation/>

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A probiotic fermented milk may help manage mild gastrointestinal discomfort in healthy female adults

Published on January, 2, 2017 by Paul Enck.



Prof. Dr. Paul Enck, Director of Research, Dept. of Psychosomatic Medicine and Psychotherapy, University Hospital Tübingen, Germany. His main interests are gut functions in health and disease, including functional and inflammatory bowel disorders, the role of the gut microbiota, regulation of eating and food intake and its disorders, of nausea, vomiting and motion sickness, and the psychophysiology and neurobiology of the placebo response, with specific emphasis on age and gender contributions.

Gastrointestinal discomfort includes different digestive symptoms such as abdominal pain, bloating, borborygmi (rumbling) and flatulence, which may impact quality of life among the general population. Probiotics can potentially improve gut function through several mechanisms and they may be an effective therapy for those with irritable bowel syndrome.

A recent systematic review and meta-analysis, led by Julie Glanville from the York Health Economics Consortium at the University of York in York (United Kingdom), has shown that the consumption of a probiotic fermented milk with *Bifidobacterium lactis* (B. lactis) CNCM I-2494 and lactic acid bacteria may improve outcomes related to mild gastrointestinal discomfort in healthy female adults.

Inclusion criteria for study selection were prospective, double-blind, randomized controlled trials that compared oral consumption of a probiotic fermented milk with a specific mix of B. lactis CNCM I-2494 and four lactic acid bacteria (*Lactobacillus bulgaricus* strains CNCM I-1632 and CNCM I-1519, *Streptococcus thermophilus* strain CNCM I-1630, and *Lactococcus lactis* ssp. *lactis* strain CNCM I-1631) with a control milk-based non-fermented dairy product for at least 4 weeks. Participants had to be 18 years old and over from the general population and with gastrointestinal discomfort at entry,

which was measured by a global assessment, using a single integrated question with a dichotomous outcome, or a composite score comprising at least two of the following individual mild digestive symptoms: abdominal pain/discomfort; abdominal pain; bloating; borborygmi; or flatulence.

A total of three randomized, double-blind, controlled, parallel-group trials with a total of 598 adults (female = 96.5%) that studied the effect of a probiotic fermented milk on gastrointestinal discomfort in the general population were included in the systematic review:

- Donazzolo *et al.*, 2007: intervention: n = 30 (37% male/63% female); control: n = 30 (33% male/67% female).
- Guyonnet *et al.*, 2009a: intervention: n = 102 (100% female); control: n = 100 (100% female).
- Marteau *et al.*, 2013: intervention: n = 168 (100% female); control: n = 168 (100% female).

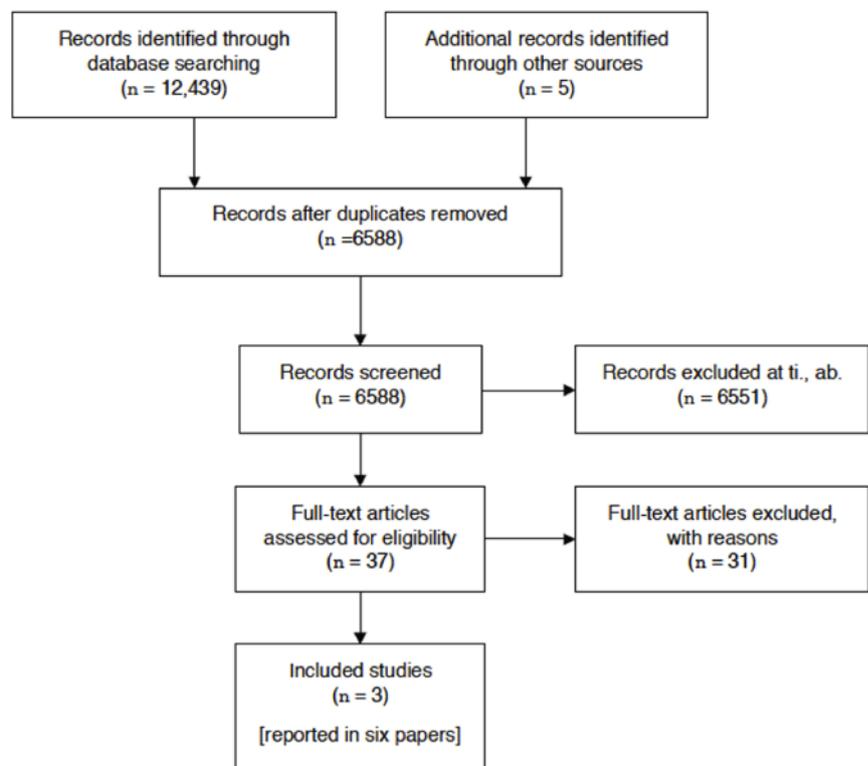
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A probiotic fermented milk may help manage mild gastrointestinal discomfort in healthy female adults

Participants who responded to the fermented milk improved bloating, abdominal pain, and borborygmi. Besides this, the lower the symptom score, the higher the probability of response (except for flatulence, as it was weakly positively related to response).

Consumption of the probiotic fermented milk product was associated with a significant improvement in overall gastrointestinal discomfort/well-being and digestive symptoms compared with the control product.

In conclusion, the consumption of a fermented milk product with *B. lactis* CNCM I-2494 and lactic acid bacteria is associated with a consistent and significant improvement of outcomes related to mild gastrointestinal discomfort in healthy adults. It must be mentioned that 96% of the studied individuals were adult women and most benefit was achieved in those with mild digestive symptoms.



CRÉDIT: EALES J ET AL. / THERAP ADV GASTROENTEROL 2016



Reference:

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Read the original post online at:

<http://www.gutmicrobiotaforhealth.com/en/probiotic-fermented-milk-may-help-manage-mild-gastrointestinal-discomfort-healthy-female-adults/>

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A new study shows probiotics can reduce depression scores and alter brain activity in humans with IBS

Published on August, 3, 2017 by Andreu Prados.



Andreu Prados holds a Bachelor of Science Degree in Pharmacy & Human Nutrition

and Dietetics. Science writer specialised in gut microbiota and probiotics, working also as lecturer and consultant in nutrition and healthcare.

Although probiotics have been reported to improve symptoms of irritable bowel syndrome (IBS), data in humans regarding their effects on psychiatric comorbidities is scarce.

A new study, led by Prof. Premysl Bercik from the Department of Medicine at the Farncombe Family Digestive Health Research Institute at the McMaster University in Hamilton (Canada), has found that the probiotic *Bifidobacterium longum* NCC3001 can reduce depression scores and increase quality of life in patients with IBS.

The researchers performed a randomized, double-blind, placebo-controlled study of 44 adults with IBS and diarrhoea or a mixed-stool pattern (according to Rome III criteria) and mild to moderate anxiety and/or depression scores based on the Hospital Anxiety and Depression (HAD) scale (HAD-A or HAD-D score 8-14). Patients were randomly assigned to the probiotic group (*B. longum* NCC3001 1.0 x 10¹⁰ colony-forming units/gram powder with maltodextrin every day; n = 22) or the placebo group

(1 gram of maltodextrin every day; n = 22) for 6 weeks. At weeks 0 and 6, patients' levels of anxiety and depression (primary outcome), IBS symptoms, quality of life and somatization (using a validated questionnaire), stool, urine, and blood samples were collected, together with an assessment of changes in brain activation patterns (using functional Magnetic Resonance Imaging, fMRI). At week 10, patients' levels of anxiety and depression, IBS symptoms, quality of life, and somatization were also determined.

Both the intervention and placebo groups had similar faecal microbiota profiles, serum markers of inflammation, and levels of neurotrophins and neurotransmitters. However, the probiotic group had reduced urine levels of the metabolites methylamines and aromatic amino acids.

Although the probiotic had no effects on anxiety or IBS symptoms, it led to a significant reduction in depression scores of 2 points or more on the HAD scale in 14/22 patients

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A new study shows probiotics can reduce depression scores and alter brain activity in humans with IBS



Although the probiotic had no effects on anxiety or IBS symptoms, it led to a significant reduction in depression scores of 2 points or more on the HAD scale in 14/22 patients. It was also shown that the beneficial effects of the probiotic on depression scores at 6 and 10 weeks was more likely to occur in those patients who reported adequate relief of IBS symptoms.

Besides this, the probiotic also led to an increase in quality of life score (measured by the SF-36 questionnaire) compared with the placebo group. At week 10, depression scores were also reduced in patients given the probiotic versus the placebo.

Regarding brain activation patterns assessed by fMRI, the probiotic

reduced responses to negative emotional stimuli in the amygdala and fronto-limbic regions, as compared with placebo. In the intervention group, reduced engagement of the amygdala correlated with decreased depression scores and was more likely to occur in those patients with adequate relief of IBS symptoms.

In conclusion, 6-week administration of *Bifidobacterium longum* NCC3001 decreased depression scores and decreased brain activity in areas involved in the processing of negative emotions. Besides this, the probiotic also improved overall symptoms of IBS and quality of life. According to the authors, "This is the first study to show that probiotics can improve depression scores as well as alter brain activity patterns in IBS patients with comorbid depression and anxiety."



Reference:

Pinto-Sanchez MI, Hall GB, Ghajar K, *et al.* Probiotic *Bifidobacterium longum* NCC3001 reduces depression scores and alters brain activity: a pilot study in patients with irritable bowel syndrome. *Gastroenterology*. 2017. doi: 10.1053/j.gastro.2017.05.003.



Read the original post online at:

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Effectiveness of probiotics in those with IBS

Published on August, 15, 2016 by Paul Enck



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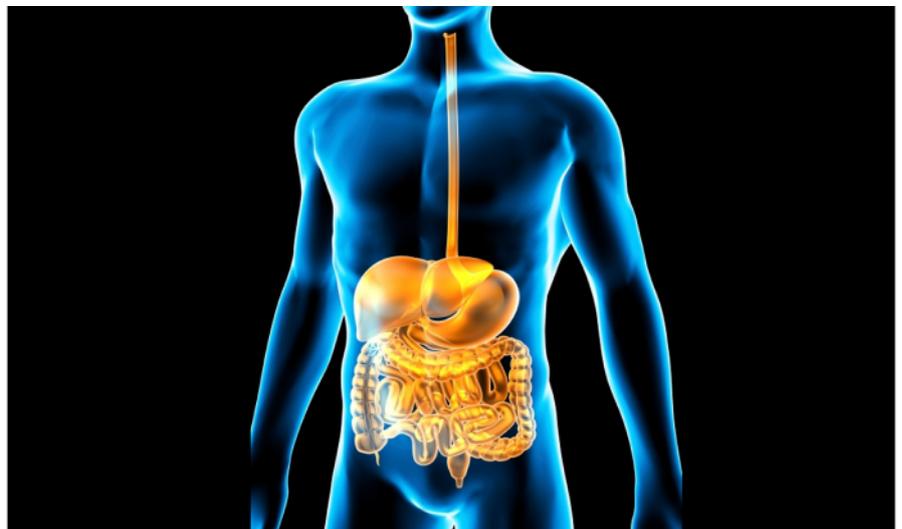
Psychotherapy, University Hospital Tübingen, Germany. His main interests are gut functions in health and disease, including functional and inflammatory bowel disorders, the role of the gut microbiota, regulation of eating and food intake and its disorders, of nausea, vomiting and motion sickness, and the psychophysiology and neurobiology of the placebo response, with specific emphasis on age and gender contributions.

Irritable bowel syndrome (IBS) is one of the most common functional gastrointestinal disorders, affecting more than 10% of the population, with the highest impact in women. Although its origin is still unknown, reduced gut microbial diversity could be involved in its development.

Clinically, IBS can only be identified by the symptoms: usually a combination of symptoms including abdominal pain or discomfort, abnormal bloating, and changes in stool frequency and consistency. Psychological factors, stress levels, lifestyle and diet reportedly affect IBS symptoms.

New therapeutic approaches with the potential to alter gut microbiota have recently been identified, and include the low fermentable, oligo-, di-, monosaccharides, and polyols (FODMAP) diet, antibiotics, and probiotics.

A recent meta-analysis of twenty-one randomized controlled trials has assessed the efficacy of different types of probiotics, doses and treatment durations in IBS patients with the Rome III criteria serving as the diagnostic criteria. It concluded that probiotic use could significantly improve overall symptoms and quality of life in IBS patients compared with placebo. No significant differences were found in the relief of individual IBS symptoms, including abdominal pain and bloating, between probiotics and placebo; this may be explained by both the ineffectiveness



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Effectiveness of probiotics in those with IBS

of administering the individual probiotics *Lactobacillus* and *Bifidobacteria* and by the different diagnostic criteria and different methods of quantifying individual IBS symptoms. Besides this, it is still unclear whether multi-species probiotics are more effective than mono-species probiotics for IBS symptoms. Regarding probiotic doses, the effect of a probiotic on the overall symptom response and quality of life seems not to be dose dependent. On the other hand, short treatment duration (less than 8 weeks) may be more effective than a long duration (8 weeks or more) for improving overall symptom response and quality of

life. On the whole, the authors conclude that probiotics at a low dose and with a short treatment duration appear to be most effective in improving overall symptom response and quality of life. The advantages of using either multi- or mono-species probiotics are still not clear.

Regarding paediatric populations, a recent multicentre, randomized, double-blind, placebo-controlled, crossover trial found that in children 8-18 years with IBS a daily mixture of a sachet consisting of 3 billion *Bifidobacterium longum* BB536, 1 billion *B. infantis* M-63, and 1 billion *B. breve* M-16V ingested for 6 weeks

was associated with improvement in abdominal pain and quality of life.

In conclusion, these results demonstrate that probiotic supplementation is an effective therapy for those with IBS. Future studies of the effects of probiotics in IBS should focus on probiotic type (multi- or mono-species probiotics), strain, dose, and treatment duration for larger populations to confirm and extend these findings.

Probiotic use could significantly improve overall symptoms and quality of life in IBS patients compared with placebo



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Giannetti E, Maglione M, Alessandrella A, *et al.* A mixture of 3 bifidobacteria decreases abdominal pain and improves the quality of life in children with irritable bowel syndrome: a multicenter, randomized, double-blind, placebo-controlled, crossover trial. *J Clin Gastroenterol.* 2016. doi:10.1097/MCG.0000000000000528.

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Read the original post online at:

<http://www.gutmicrobiotaforhealth.com/en/effectiveness-probiotics-ibs/>

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Group investigates the value of probiotics in reducing inappropriate antibiotic use

Published on February, 6, 2017 by Kristina Campbell.



Science writer Kristina Campbell (M.Sc.), from British Columbia (Canada), specializes in communicating about the gut microbiota, digestive health, and nutrition. Author of the best selling *Well-Fed Microbiome Cookbook*, her freelance work has appeared in publications around the world. Kristina joined the Gut Microbiota for Health publishing team in 2014.

Antibiotics are a crucial part of the medical toolbox, but their clinical benefit for patients must be balanced against possible adverse drug reactions and increased risk of *Clostridium difficile* infection (CDI). Studies indicate between one quarter and one half of all antibiotics prescribed in US acute care hospitals are either unnecessary or inappropriate. Widespread antibiotic misuse has also contributed to the problem of antimicrobial resistance (AMR), a serious public health threat that continues to grow. AMR occurs when microorganisms change in ways that render antibiotics ineffective at killing them or controlling their growth. An estimated 23,000 deaths in the US annually are attributable to infection with antibiotic-resistant organisms; according to the World Health Organization, “AMR is an increasingly serious threat to global public health that requires action across all government sectors and society.”

These points have led to the worldwide emergence of hospital-based antibiotic stewardship programs (ASPs)—coordinated strategies to limit inappropriate and excessive antibiotic use. In addition to reducing antibiotic resistance, such programs aim to improve patient health outcomes (through increased infection cure rates, reduced treatment failures, and correct therapeutic and prophylactic prescriptions) while decreasing unnecessary costs. In 2014, the CDC recommended all acute care hospitals implement ASPs, and subsequently outlined the core elements of successful programs.

Members of the scientific community have raised the idea of whether, given current scientific evidence, probiotics can be a tool employed in ASPs and other initiatives

for reducing inappropriate use of antibiotics. In practice, the drugs are often used improperly to address common infections caused by viruses, leading some experts wonder whether probiotics may be used prophylactically to reduce the occurrence of infections in the first place, or render them less severe.

“Prevention is always preferred to treatment,” says Mary Ellen Sanders, Executive Science Officer for the International Scientific Association for Probiotics and Prebiotics (ISAPP). “If we prevent infections, antibiotics can be fully avoided.”

At the 2016 ISAPP meeting in Turku, Finland, a working group, led by Dan Merenstein of Georgetown University (USA) and Irene Lenoir-Wijnkoop of University of Utrecht (the Netherlands) and Danone

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Group investigates the value of probiotics in reducing inappropriate antibiotic use

Research, laid out the strength of evidence to support probiotics in reducing the incidence and severity of upper respiratory tract infections (URTIs)—the common cold.

A 2015 Cochrane meta-analysis of 12 studies indicated evidence is accumulating, but not definitive, for probiotics in improving outcomes related to URTIs: probiotic use resulted in 11 fewer people out of 100 developing an URTI, and reduced the duration of a URTI by around 2 days. Yet it was clear that the use of probiotics was associated with lower antibiotic prescription rates for acute URTIs.

Health-economic analyses of specific countries, published in 2015 and 2016, showed that widespread probiotic consumption could potentially save hundreds of thousands of antibiotic prescriptions per year (between 291,000 and 473,000 in France; between 52,000 and 84,000 in Canada) and beget significant healthcare cost savings through their impact on URTIs.

Missing from the literature is a systematic review of randomized,



controlled trials to examine the overall impact of probiotics on inappropriate antibiotic prescriptions within the context of common acute infections. ISAPP members and collaborators have now initiated such a review, addressing the question: Is the use of antibiotics reduced when people are given probiotics to prevent or treat common acute infections?

“This research question was chosen because studies on common acute

infections are the ones that report on antibiotic prescription use,” says Sanders, an author on the systematic review protocol.

The protocol has been registered with PROSPERO (registration number CRD42016052694) and is scheduled to be published within the next year.



Read the original post online at:

<http://www.gutmicrobiotaforhealth.com/en/group-investigates-value-probiotics-reducing-inappropriate-antibiotic-use/>

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An updated guide with strengthened evidence to help clinicians use probiotics in the management of lower gastrointestinal symptoms

Published on February, 26, 2018 by GMFH Editing Team

Gut-related symptoms, including flatulence, bloating, heartburn, nausea, vomiting, constipation, diarrhoea, food intolerance, incontinence, and abdominal pain affect approximately one third of the general population, according to the World Gastroenterology Organisation. Among the functional gastrointestinal disorders (FGIDs) that are characterized by persistent and recurring GI symptoms, irritable bowel syndrome (IBS) affects around 11% of the population globally and can interfere with everyday activities and quality of life.

Evidence suggests that the gut microbiota play an important role in gastrointestinal disorders. Probiotics in the context of personalized dietetic recommendations may affect many GI disorders through their ability to alter the dysbiotic gut microbiota or change patients' tolerance to their own commensal gut microbiota. Several randomized controlled trials support the efficacy of probiotics as a coadjuvant treatment in different functional bowel disorders in both paediatrics and adult populations.

As gastrointestinal and digestive disorders account for one in 10 consultations in primary care, healthcare practitioners face the challenge of finding evidence-based information on how to prevent lower GI symptoms and decide which probiotic to recommend—which strain and formulation, at what dose, using what mode of administration, and for how long. Besides this, it is not possible to extrapolate the results of a particular study with one species of probiotic, one dose, and one formulation in one GI disorder to other probiotics.

Therefore, there is a need for guidelines and advice for prescribing probiotics in clinical practice for GI disorders.

A recent systematic review, led by Prof. Pali Hungin from the School of Medicine and Health at Durham University and on behalf of the European Society for Primary Care Gastroenterology, provides an update

on the use of probiotics in the treatment of lower GI symptoms in adults.

By compiling data from January 2012 to June 2017, the authors included a total of 70 randomised, placebo-controlled trials (RCTs) (33 newly identified studies in addition to 37 publications in the original review published in 2013).



SELECTED CONTENT

An updated guide with strengthened evidence to help clinicians use probiotics in the management of lower gastrointestinal symptoms

Indications examined were irritable bowel syndrome (IBS), 34 studies; diarrhoea associated with antibiotics, 13 studies; diarrhoea associated with *Helicobacter pylori* eradication therapy, 7 studies; other conditions, 16 studies. The new review covers the role of probiotics in patients with other GI conditions, such as healthy individuals with minor GI complaints, patients with lactose intolerance and those receiving antibiotics or undergoing *H. pylori* eradication therapy.

The Delphi method was employed. An eight-expert panel voted on 13 previously developed statements until agreement of >67% was reached. The level of supporting evidence and strength of each statement was rated using the GRADE system.

Collectively, the 70 studies investigated a total of 54 different probiotic products (containing 108 strains either alone or in combination) at doses ranging from 1×10^6 to 4.5×10^{11} colony forming units (CFU) per day, administered as one, two or three doses. They predominantly contained bacteria (mostly lactobacilli and/or bifidobacteria); a few contained the yeast *Saccharomyces*.

With a grade of evidence for effect being “high”, specific probiotics may help relieve overall symptom burden in some patients with IBS. Among 15 studies that evaluated overall symptoms as a primary endpoint in patients with IBS, 8 studies reported a significant beneficial effect of 8 different probiotic products (dosed at 3.4×10^7 to 2.5×10^{10} CFU per day) compared with placebo. However, the grade of evidence for the use of specific probiotics in relieving overall symptom burden in patients with constipation-predominant IBS and patients with diarrhoea-predominant IBS was very low and low, respectively.

Regarding abdominal pain, among 9 studies that evaluated abdominal pain as a primary endpoint, 7 studies showed a significant beneficial effect of specific probiotic treatments compared with placebo in some patients with IBS with a high grade of evidence.

On the other hand, probiotics showed a moderate grade of evidence in reducing bloating/distension in some patients with IBS. The role of probiotics in reducing flatus in patients with IBS is still unclear.

Although probiotics showed a moderate grade of evidence for improving frequency and/or consistency of bowel habits in some patients with IBS, its role for relief of constipation had low evidence.

In patients receiving antibiotic therapy or *H. pylori* eradication therapy, specific probiotics at doses of between 2×10^6 to 2×10^{10} CFU per day appeared helpful as adjuvant therapies to prevent or reduce the duration of associated diarrhoea, with a high grade of evidence. Based on 13 studies of 10 different probiotics in 6091 patients who received antibiotics, probiotics were helpful as adjuvant therapy to prevent or reduce the duration of antibiotic-associated diarrhoea.

Regarding adverse events, probiotics have a favourable safety profile in patients with a range of lower GI symptoms typically managed in primary care.

There is a need for guidelines and advice for prescribing probiotics in clinical practice for GI disorders

SELECTED CONTENT

An updated guide with strengthened evidence to help clinicians use probiotics in the management of lower gastrointestinal symptoms

The following table summarizes practical implications of the consensus statement for healthcare practitioners:

| Grade of evidence for effect | Indications | Clinical translation |
|------------------------------|--|---------------------------------|
| High | <ul style="list-style-type: none"> > Overall symptoms and abdominal pain in IBS. > Prevention or reduction of diarrhoea in patients receiving antibiotics or <i>Helicobacter pylori</i> eradication therapy. | Probiotics should be tried. |
| Moderate | Bowel movements and bloating and distension in IBS. | Probiotics could be tried. |
| Low | <ul style="list-style-type: none"> > Overall symptoms in IBS-D. > Flatus in IBS. > Constipation in IBS. | Probiotics could be considered. |
| Very low | <ul style="list-style-type: none"> > Overall symptoms in IBS-C. > Diarrhoea in IBS. | No evidence. |

In conclusion, this updated review indicates that specific probiotics are beneficial in relieving lower GI symptoms in IBS and preventing diarrhoea in patients prescribed antibiotics or H. pylori eradication therapy.

The expert consensus panel concluded the review with the following pragmatic recommendations for clinicians:

- Specific probiotics have a role in the management of IBS in some cases and can also be used as an adjunct to conventional treatment.
- Probiotic strains should be selected based on the patient's symptoms, the clinical indication and the available evidence; no probiotic alleviates the full range of symptoms in IBS.
- When trying a probiotic therapy for a chronic GI problem, the product should be taken at least for 1 month; dose selection should be based on available evidence and manufacturers' recommendations.



Reference:

Hungin APS, Mitchell CR, Whorwell P, *et al.*; for the European Society for Primary Care Gastroenterology. Systematic review and consensus: probiotics in the management of lower gastrointestinal symptoms in clinical practice – an updated evidence-based international guide. *Aliment Pharmacol Ther.* 2018; 00:1-17. doi: 10.1111/apt.14539.



Read the original post online at:

<http://www.gutmicrobiotaforhealth.com/en/updated-guide-strengthened-evidence-help-clinicians-use-probiotics-management-lower-gastrointestinal-symptoms/>

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