Gut microbiota: underestimated or exaggerated?

Bağırsak mikrobiyotası: Küçümsenmiş mi, abartılı mı?

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Abstract

Human gastrointestinal tract contains a large diversity of commensal microorganisms, which is many times more than the human living cells. In the last decade, we had enormous number of research on the association with diseases and gut microbiota composition. There is a clear increase in the number of pathological conditions associated with dysbiosis in time. Also, the range of diseases are increased and distributed to many disciplines, non-gastrointestinal diseases are also increasingly reported. Gut microbiota has multiple functions and new applications for diagnosis and therapeutics of diseases. Probiotics are widely used in health and disease states. Probably further high quality scientific research will determine the exact place of gut microbiota and probiotics in human health in the future.

Key words: *gut microbiata, probiotics*

Özet

İnsan gastrointestinal sistemi, tüm insan hücrelerine göre çok daha fazla sayıda ve büyük bir çeşitlilikteki komensal mikroorganizmaları içerir. Son on yılda, bağırsak mikrobiyotasının içeriği ve hastalıkların ilişkisi üzerine çok fazla sayıda araştırma yaptık. Zaman içinde disbiyoz ile ilişkili patolojik durumların sayısında belirgin bir artış olmuştur. Ayrıca, bu hastalıkların yelpazesi daha da genişlemiş ve birçok disipline dağılmıştır. Gastrointestinal hastalıklar dışındakiler giderek daha fazla rapor edilir olmuştur. Bağırsak mikrobiyatası birçok fonksiyona sahip olmanın yanında hastalıkların tanı ve tedavisi için de birçok yeni uygulamaya sahiptir. Probiyotikler, hastalık ve sağlıkta yaygın olarak kullanılmaktadır. Yüksek kaliteli bilimsel araştırmalar, gelecekte bağırsak mikrobiyotası ve probiyotiklerin insan sağlığı üzerindeki gerçek yerini belirleyecektir.

Anahtar kelimeler: *bağırsak mikrobiyotası, probiyotikler*

Introduction

Human gastrointestinal tract contains a large diversity of commensal microorganisms, which is many times more than the human living cells.[1-3] During the pregnancy, infant's intestinal tract is free of microbes until exposed to maternal vaginal microbes during normal birth.[4] Infants born through Caesarian section are exposed to maternal skin bacteria altering their bacterial gut composition.[5] Although some researchers have suggested that the number of

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microbes in the human gut is tenfold the total number of human somatic cells, a recent estimate has calculated that the numbers are of the same order, with the total number of bacteria in the human body being around 3.8×10^{13}.[6] In the last decade, we had enormous number of research on the association with diseases and gut microbiota composition. As the fog on the topic clears, we are able to see the solid evidence behind claims of microbiota and health. In the first years of microbiota research, many diseases had associations with gut microbiota disturbances (dysbiosis) (Table 1).

There is a clear increase in the number of pathological conditions associated with dysbiosis in time. Also, the range of diseases are increased and distributed to many disciplines. Non-gastrointestinal diseases are also increasingly reported. However, this is only association and not causation. Extreme care should be given not to extrapolate these findings to clinical scenarios.

Animal models (mostly germ-free rats) were used to study the association and later etiological impact of dysbiosis in a certain disease. Fecal transplantation from the pathological animal to germ-free rat induces dysbiosis and subsequent pathological events. Although this model is widely reported, we should be careful in interpreting the results. These animals are not human alike. Rats are coprophagic and share mostly the same environment (although in separate cages). Diet is not rich as in humans and there are few factors affecting gut microbiota in laboratory conditions. Humans live in a big community, they eat, drink, exercise, travel, etc. However, in "proof of concept" studies, we have some evidence from animal studies.

The clinical effects of microbiota is mediated by metabolites such as short-chain fatty acids (SCFAs), and the gases hydrogen sulfide, ammonia, hydrogen, methane, carbon monoxide and carbon dioxide.[7] SCFAs, are mainly butyrate, propionate and acetate. They are produced under anaerobic conditions in the large intestine by fermentation of dietary fibers. SCFAs, especially butyrate, has anti-inflammatory effects in the gut.[8]

Table 1. Diseases associated with dysbiosis

Year 2011	Year 2018
Atopy and Asthma	Colorectal cancer
Celiac disease	Autism
Colon cancer	Atherosclerosis
Type 1 and 2 diabetes mellitus	Mood disorders
HIV infection	Multiple sclerosis
IBD	Non-alcoholic fatty liver disease
IBS	Cirrhosis and complications
Gastroenteritis	Psoriasis
Necrotizing enterocolitis	Gastric cancer
Obesity	Celiac disease
Rheumatoid arthritis	Alcoholic hepatitis
	Chronic fatigue syndrome

IBD : Inflammatory Bowel Disease
IBS : Irritable Bowel Syndrome

Probiotics

Up to now, several bacteria and fungi species have been used for human health. Several bacterial species and their role as a positive probiotic agent have been evaluated such as *Lactobacillus* and *Bifidobacterium* species. Accordingly, *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces boulardii* are the most common bacterial and fungal species participating as probiotics. The term probiotics is defined by a United Nations and World Health Organization Expert Panel as "live microorganisms which when administered in adequate amounts confer a health benefit on the host".[9]

The quality of probiotic products depends on the manufacturer concerned. Since most are not made to pharmaceutical standards, the regulatory authorities may not oversee adherence to quality standards. The issues that are important specifically for probiotic quality include maintenance of viability (as indicated by colony-forming units, or CFU) through the end of the product's shelf-life and using the current nomenclature to identify the genus, species, and strain of all organisms included in the product.[10]

Evidence based clinical applications of probiotics in adults:[11-55]

- Treatment of acute diarrhea in adults
  - (Lactobacillus paracasei B 21060 or L. rhamnosus GG, Saccharomyces boulardii CNCM I-745)
- Antibiotic-associated diarrhea
  - (Lactobacillus casei DN114, L. bulgaricus, and Streptococcus thermophilus, Lactobacillus acidophilus CL1285 and L. casei, Lactobacillus rhamnosus GG, Saccharomyces boulardii CNCM I-745, Lactobacillus reuteri DSM 17938, Lactobacillus acidophilus NCFM, L. paracasei Lpc-37, Bifidobacterium lactis Bi-07, B. lactis Bl-04)
- Prevention of Clostridium difficile–associated diarrhea (or prevention of recurrence)
  - (Lactobacillus acidophilus CL1285 and L. casei LBC80R, Lactobacillus casei DN114 and L. bulgaricus and Streptococcus thermophilus, Saccharomyces boulardii CNCM I-745, Lactobacillus rhamnosus HN001 + L. acidophilus NCFM, Lactobacillus acidophilus + Bifidobacterium bifidum)
- Coadjuvant therapy for HP eradication
  - (Lactobacillus rhamnosus GG, Bifidobacterium animalis subsp. lactis (DSM15954), Lactobacillus rhamnosus GG, Lactobacillus reuteri DSM 17938, Saccharomyces boulardii CNCM I-745, Bacillus clausii, Lactobacillus reuteri DSM 17938 and L. reuteri ATCC 6475)
- Hepatic encephalopathy
  - VSL#3 (mixture of eight strains: 1 Streptococcus thermophilus, 4 Lactobacillus, 3 Bifidobacterium), Nonabsorbable disaccharides (lactulose), Yogurt with Streptococcus thermophilus, Lactobacillus bulgaricus, L. acidophilus, bifidobacteria, and L. casei)
- Non-alcoholic fatty liver disease
  - (Yogurt (with Lactobacillus bulgaricus and Streptococcus thermophilus) enriched with L. acidophilus La5 and Bifidobacterium lactis Bb12, Mixture of Lactobacillus casei, L. rhamnosus, Streptococcus thermophilus, Bifidobacterium breve, L. acidophilus, B. longum, and L. bulgaricus + fructo-oligosaccharides)
- Irritable Bowel Syndrome
  - (Bifidobacterium bifidum MIMBb75, Lactobacillus plantarum 299v (DSM 9843), Escherichia coli DSM17252, Lactobacillus rhamnosus NCIMB 30174, L. plantarum NCIMB 30173, L. acidophilus NCIMB 30175, and Enterococcus faecium NCIMB 30176., Bacillus coagulans and fructo-oligosaccharides, Lactobacillus animalis subsp. lactis BB-12®, L. acidophilus LA-5®, L. delbrueckii subsp. bulgaricus LBY-27, Streptococcus thermophilus STY-31, Saccharomyces boulardii CNCM I-745, Bifidobacterium infantis 35624, Bifidobacterium animalis DN-173 010 in fermented milk (with Streptococcus thermophilus and Lactobacillus bulgaricus), Lactobacillus acidophilus SDC 2012, 2013, Lactobacillus rhamnosus GG, L. rhamnosus LC705, Propionibacterium freudenreichii subsp. shermanii JS DSM 7067, Bifidobacterium animalis subsp. lactis Bb12 DSM 15954, Bacillus coagulans GBI-30, 6086, Pediococcus acidilactici CECT 7483, Lactobacillus plantarum CECT 7484, L. plantarum CECT 7485).

In conclusion, gut microbiota has multiple functions and new applications for diagnosis and therapeutics of diseases. Probiotics are widely used in health and disease states. Physicians are divided into discrete opinions for the use of probiotics. Most of them are waiting for more solid evidence to implement them into daily practice. Probably further high quality scientific research will determine the exact place of microbiota and probiotics in human health in the future.

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