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Probiotics and prebiotics in infectious gastroenteritis

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A B S T R A C T

Acute gastroenteritis (AGE) is worldwide a common problem in infants and children. While AGE is still an important cause of morbidity and mortality in developing countries, it is mainly a problem with high socioeconomic impact in the rest of the world. Oral rehydration solutions (ORS) and rapid refeeding remain the cornerstone of the management. However, ORS does not decrease the duration of diarrhea. There is evidence that selected strains of probiotics decrease the duration of AGE with 24 h, both in ambulatory care and in hospitalized children, resulting also in a decrease of the duration of hospitalization. Synbiotics are equally effective as probiotics alone, but prebiotics are not effective. Both pro- and prebiotics have limited to no efficacy in the prevention of AGE. The administration of pre- and probiotics is considered to be safe, even in newborns. Only these pre-, pro and synbiotics that have been clinically tested can be recommended.

Introduction

Prebiotic oligosaccharides are non-digestible food ingredients that stimulate the growth and/or activity of bacteria in the digestive system in ways claimed to be beneficial to health. Prebiotics were first identified and named by Marcel Roberfroid in 1995. A prebiotic is a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microbiota that confers benefits upon host well-being and health.

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The word "probiotic" was used for the first time in the 1960s and means "for life" (from the Greek *προ βίος*, *pro bios*). Probiotics are live microorganisms that, when administered in adequate amounts, confer a health benefit on the host. There are bacterial and yeast probiotics. The best known bacterial probiotics are lactobacilli and bifidobacteria. *Saccharomyces boulardii* is a non-pathogenic yeast isolated from the lychee fruit and introduced in France for the treatment of diarrhea since 1950. The major indications of probiotics are in the area of the prevention and treatment of gastro-intestinal (GI) related disorders. The number of commercialized products and the number of publications on probiotics in different conditions has literally exploded during recent years. It is accepted that at least two published randomized controlled trials with a commercialized product in the claimed indication are a minimal condition before a claim can be sustained.

The commercialized products

There are no commercialized prebiotic products for the prevention or treatment of acute gastroenteritis (AGE).

Quality control of the commercialized probiotic products is fundamental [1]. Most probiotics are registered as food supplement and do not have to fulfill the regulations and quality requirements that exist for medication. The product label is incorrect in almost half of the probiotic food supplements [2]. Companies can refuse to provide information on the exact strains in the product [3]. Fundamental research on the mechanisms of action of specific strains and clinical trials with commercialized products are mandatory since in vitro effects of a strain may display opposite behavior in vivo [4].

Most used bacterial probiotic strains comprise different lactobacilli (L.) (*Lactobacillus casei* GG, *Lactobacillus reuteri* DSM 17938, *L.* LA5, …) and bifidobacteria (B.) (*Bifidobacterium lactis*, *Bb12*, …), but also to a certain extent non-pathogenic *Escherichia (E.) coli* (*E. coli* Nissle 1917). The yeast *Saccharomyces (S.) boulardii* CNCM I-745 is the only non-bacterial probiotic strain evaluated in acute gastroenteritis.

Probiotic products in prevention and treatment

Prevention of acute infectious diarrhea

The study by Saavedra et al. published in 1994 demonstrating that *Streptococcus (Str.) thermophilus* and *Bifidobacterium bifidum* (later renamed *B. lactis*) prevent nosocomial acquired diarrhea in a small group of children admitted in a chronic care institution can be considered as the kick-off study [5].

Since then many studies have been performed with different probiotic strains, with different amounts, added to infant formula or administered separately to evaluate the efficacy of probiotics in the prevention of AGE. Large, randomized controlled trials (RCT), meta-analyses and reviews provide evidence for a very modest effect (statistically significant, but of questionable clinical importance) of some probiotic strains in the prevention of community-acquired diarrhea [6–10].

The American Academy of Pediatrics concluded in 2010: "available data do not support routine use of probiotics to prevent nosocomial rotavirus diarrhea in child care centers. But, there may be special circumstances in which probiotic use in children in long-term health care facilities or in child care centers is beneficial" [11]. The European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) concluded one year later that there was "insufficient evidence to recommend the use of infant formula enriched with probiotics mainly because the efficacy shown was insufficiently convincing" [12]. However, some studies do show benefit although for different endpoints and the benefit is not always statistically significant. There are also negative studies [13]. Recently, *Bifidobacterium animalis* subsp. *lactis* was shown to fail to prevent common infections in hospitalized children [13]. Preliminary data suggest that *L. reuteri* may be effective in the prevention of some functional gastrointestinal disorders, such as colic and regurgitation, but AGE was not evaluated [14].

Serious adverse events of probiotics added to infant formula were not reported.

In summary: there is insufficient evidence to recommend probiotics to prevent AGE in dally routine (added to infant formula) or in at risk situations, such as during hospitalization for an acute disease. However, no study reported a negative outcome. Studies show either a trend of some benefit compared to placebo, or studies show no difference, but no study has a negative outcome. Therefore, the strategy