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REVIEW ARTICLE

An update on probiotics, prebiotics and symbiotics in clinical nutrition[☆]

Gabriel Olveira^{a,b,*}, Inmaculada González-Molero^{a,b}^a UGC Endocrinología y Nutrición, Instituto de Investigación Biomédica de Málaga, Hospital Regional Universitario de Málaga, Universidad de Málaga, Málaga, Spain^b CIBERDEM, Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas (CB07/08/0019), Instituto de Salud Carlos III, Madrid, Spain

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Abstract The concept of prebiotics, probiotics, and symbiotics and their use in different situations of daily clinical practice related to clinical nutrition is reviewed, as well as their role in the treatment/prevention of diarrhea (acute, induced by antibiotics, secondary to radiotherapy), inflammatory bowel disease (ulcerative colitis and pouchitis), in colonic health (constipation, irritable bowel), in liver disease (steatosis and minimum encephalopathy), and in intensive care, surgical, and liver transplantation. While their effectiveness for preventing antibiotic-induced diarrhea and pouchitis in ulcerative colitis appears to be shown, additional studies are needed to establish recommendations in most clinical settings. The risk of infection associated to use of probiotics is relatively low; however, there are selected groups of patients in whom they should be used with caution (as jejunal infusion).

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PALABRAS CLAVE

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Resumen Se revisa el concepto de prebióticos, probióticos y simbióticos y su empleo en diferentes situaciones de la práctica clínica diaria relacionados con la nutrición clínica. Se analiza su papel en el tratamiento y/o prevención de la diarrea (aguda, por antibióticos,

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* Corresponding author.

E-mail address: gabrielm.olveira.sspa@juntadeandalucia.es (G. Olveira).

rádica), en la enfermedad inflamatoria intestinal (colitis ulcerosa y reservoritis), sobre la salud colónica (estreñimiento, intestino irritable), hepatopatías (esteatosis y encefalopatía mínima), en pacientes de cuidados intensivos, quirúrgicos y sometidos a trasplante hepático. Si bien parece demostrada su eficacia en la prevención de la diarrea por antibióticos y en la reservoritis en la colitis ulcerosa, son necesarios más estudios para poder establecer recomendaciones en la mayoría de escenarios clínicos. El riesgo de infección asociado al uso de probióticos es relativamente bajo; no obstante, existen grupos seleccionados de pacientes en los que se recomienda emplearlos con cautela (como la infusión a nivel yeyunal).

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Introduction

The luminal surface of the bowel contains billions of living microorganisms in a number approximately ten times higher than the number of cells in an adult person. Most of them are located in the colon, where certain bacterial species reside. The human bowel is, therefore, a true ecosystem essential for the efficient absorption of nutrients and for the maintenance of health in general. In a Persian version of the Old Testament, the longevity of Abraham is attributed to the consumption of "sour milk". As early as 76 AD, the Roman historian Pliny recommended fermented dairy products for the treatment of gastroenteritis. In 1908, the Nobel Prizewinner Elie Metchnikoff attributed the longevity of some Balkan populations to their regular consumption of fermented dairy products containing lactobacilli that "reduce the toxins produced by intestinal bacteria, promoting health and prolonging life". At the beginning of the 20th century, it was reported that the bacterium *Lactobacillus acidophilus* was able to survive in the human bowel.

It appears that hominids started to use lactic acid fermentation of plant foods approximately 1.5 million years ago. This was a common practice in Europe until the industrial revolution, and continues to be regularly used by various African communities because it is a safe and simple way to preserve food. The intake of fermented dairy products by humans possibly started more recently (some 10,000 years ago). Over time, the hominid gastrointestinal tract gradually adapted to a generally high daily provision of live lactic acid bacteria. This type of food stopped being eaten in industrialized countries during the 20th century, which may have caused different gastrointestinal and immunological problems. In the 1980s, it was postulated that some indigestible components of the diet could promote the growth of certain bacterial strains present in the bowel which are associated with benefits for health.¹

Concept of probiotics, prebiotics, and symbiotics

While the initial definition of probiotics proposed in 1965 referred to substances secreted by microorganisms that stimulate the growth of others (in contrast to "antibiotics"),^{2,3} the WHO definition of "probiotic" refers

to live microorganisms which, when administered in adequate amounts, have a beneficial effect on the health of the host.⁴ According to the International Scientific Association for Probiotics and Prebiotics, the spectrum of products and preparations that may be considered as probiotics is very wide (Fig. 1) and extends from probiotic drugs (e.g. VSL#3), foods for special medical uses with probiotics (e.g. enteral nutrition with probiotics), probiotic foods (e.g. fermented milk with studies showing benefits for health), and infant formulas (e.g. milk powders) to non-orally administered probiotics (e.g. vaginal). To be considered a probiotic, studies should have been conducted in humans effectively showing the specific health benefits of specific strains (e.g. *Lactobacillus rhamnosus* GG; not only of the genus *Lactobacillus* or the species *rhamnosus*).³ Fermented food containing live organisms often does not meet the concept of probiotics if its effects have not been specifically studied and/or the amount it contains is not known. By contrast, some fermented food products such as yoghurt can be considered in some circumstances as probiotics based on some specific effects. For example, if there is evidence that they improve lactose digestion in subjects with lactose intolerance; the benefits do not only depend on the lower lactose content of the product, but also on the fact that probiotic bacteria can also increase lactase activity in the small bowel.

Fecal transplant or foods with dead microorganisms are not considered as probiotics.²

To produce the beneficial effects in the host, probiotics do not need to colonize the target organ, but it should be reached by a sufficient number of live microorganisms so as to affect its microecology and metabolism. Thus, most probiotic strains are able to reach the colon alive (in a variable percentage) after passing through the upper gastrointestinal tract, and their viability depends on many factors: intrinsic probiotic factors on the one hand and, on the other, host-dependent factors such as, for example, stomach acidity, the length of acid exposure, the concentration and duration of exposure to bile salts, and others.⁵ To give an example, the strains *Lactobacillus casei* Shirota, *L. rhamnosus* GG (ATCC 53103), *Lactobacillus johnsonii* LA1, and *L. acidophilus* NCFB 1748 have been shown to be safe and to have benefits for health in humans, and also to have high stability in acid media and to be resistant to bile acids; however, only the last three strains are able to adhere to the mucosa and only *L. rhamnosus* GG and *johnsonii*LA1 induce colonic colonization.⁶

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