

Probiotics and Prebiotics for Prevention of Food Allergy: Indications and Recommendations by Societies and Institutions

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ABSTRACT

Probiotics are defined as “live microorganisms that, when administered in adequate amounts, confer a health benefit on the host”. Unfortunately, misuse of the term probiotic is very common. According to the regulation of the European food safety authority (EFSA) health claims on pre- and probiotics are not judged as favorable. Scientific societies should give guidance to the consumers and health care professionals on the use of probiotics and prebiotics for prevention and disease management. There is currently no positive recommendation from international scientific medical societies to use prebiotics or probiotics for treatment of food allergy or other allergic manifestations and for prevention of food allergy, allergic rhinitis, and asthma. Discrepant recommendations exist for probiotics for prevention of eczema in high risk infants.

Key Words: atopic eczema, guidelines, health claim, randomized controlled trials

INTRODUCTION

In 2001 the FAO/WHO defined probiotics as “live microorganisms that, when administered in adequate amounts, confer a health benefit on the host”. This definition has been widely adopted by regulatory agencies such as Codex alimentarius, and the European Food Safety Authority (EFSA), scientists, industry, and consumers. The definition translates into scientific terms that a specific probiotic strain should have been investigated in properly controlled studies to confer a specific benefit before a claim with respect to this benefit can be made. If this is not fulfilled the only allowed claim would be “contains probiotics”. In an extensive review on health claims on probiotics and prebiotics in Europe van Loveren et al. concluded that studies using probiotics or prebiotics have generally been designed as exploratory and were not sufficiently designed to fulfill the criteria for substantiation of a health claim under the current claims regulation by EFSA (1).

In 2014 the International Scientific Associations for Probiotics and Prebiotics published a consensus statement on the scope and appropriate use of the term probiotic (2). In their manuscript the authors describe the objectives of four main stakeholders in the field of probiotics. In the “ideal world” the scientists want to generate high-quality science that has a positive impact on the society, while the goal of the industry is to market a high-quality profitable product with validated and understandable claims. The consumer wants reliable information to make informed decisions what to buy while the task of the regulator is to protect the consumers

from misinformation. The role of Scientific Societies is to give guidance not only to the consumers, but also to health care providers in the different field. Unfortunately, the world of science is not always ideal, and publications in the field of probiotics are often not of high quality or free of competing interests of the investigators. Since probiotics are not considered as food supplements, regulation to perform such studies are less strict compared to drug trials which have to follow the rules and regulations of the national drug agencies and regulatory bodies which require external monitoring and other control mechanism described as “good clinical practice” (GCP).

In order to recommend probiotics for allergy prevention it needs to be proven that a specific probiotic bacterium or a mixture of probiotic strains given to the pregnant or breastfeeding mother or directly to the infant or young child reduces the risk of later allergies. Scientific societies have a specific responsibility to consider the different aspects, the quality and reliability of studies using probiotics when formulating recommendations and indications for their use. Although systematic reviews and meta-analysis in this field are very frequent, and sometimes outnumber the number of original studies, they are often not helpful or even misleading because they sometimes pool studies using different strains and/or with very poor, moderate or good quality.

Questions Addressed Regarding Study Protocols Using Probiotics for Allergy Prevention (PICOS)

- Population of interest
 - To the general population or to high allergic risk population?
 - To the pregnant mother or the offspring?
- Intervention(s) received
 - Strain, dose, application, duration etc.
- Comparator
 - None, placebo, other probiotic
- Outcome(s)
 - Food allergy, eczema, sensitization, asthma etc.
- Study type
 - RCT, Placebo controlled, observational, retrospective, prospective etc.

An example for a differential outcome in two different populations (Finland and Germany) are the two studies applying the identical probiotic strain (*Lactobacillus rhamnosus GG*) to pregnant women and their infants with a very similar study design (3,4). While the Finish study showed a significant risk reducing effect on atopic eczema of the probiotic compared to placebo (3), the German study did not (4). What are the consequences for recommendations with so controversial outcomes: to support the use in Finland, but not in other countries or not to recommend at all, since significance is lost when the data are pooled (5). Wickens et al randomized almost 500 mother- infant pairs with high risk for allergies to two different probiotics and placebo (6). The infants were followed until 2 years of age for occurrence of eczema and atopy. While one probiotic reduced the risk for eczema compared to placebo, the other did not. In a later study they genotyped the participants for 54 SNPs in the toll-like receptor genes and speculated based on their findings that the different probiotic strains may act differently depending on the genotype (7). While their finding is scientifically very interesting it makes it difficult to recommend certain interventions if the benefits depends on the genotype.

With respect to outcome most studies have looked at atopic eczema as a primary endpoint, since this is the most frequent allergic manifestation during the first years of life (6–8), while

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allergies in the respiratory tract (asthma and allergic rhinitis) follows later during school age and adolescence and are difficult to study in randomized prospective intervention trials (9,10). While clear criteria for the diagnosis of eczema, asthma and allergic rhinitis exist, the diagnosis of food allergy is more difficult. It requires a strict elimination and challenge procedure which needs to be double blind in most cases with IgE positivity and all with negative results of specific IgE tests for the suspected food (11). So far no randomized controlled trial with probiotics or prebiotics used strict diagnostic criteria for food allergy.

Recommendations by Scientific Medical Societies

As the consequence of lack of evidence several international and national scientific societies do not support the use of probiotics or prebiotics for the prevention or management of food allergy or other allergic manifestations.

- The European Academy of Allergy and Clinical Immunology (EAACI) stated 2014 in their food allergy and anaphylaxis guidelines on primary prevention of allergy, that “there is no evidence to recommend prebiotics or probiotics or other dietary supplements based on particular nutrients to prevent food allergy” in at risk groups and in the general population (grade of recommendation B) (12).
- With respect to treatment of manifest food allergy the EAACI concluded 2014 in their guidelines on diagnosis and management of food allergy that “probiotic supplements cannot be recommended for the management of food allergy (grade of recommendation D) (13).
- The Nutrition Committee of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) concluded 2011 after a systematic literature review on the effect of infant formula supplemented with prebiotics or probiotics on the preventive effect on allergy, that “there is too much uncertainty to draw reliable conclusions from the available data”.
- The World Allergy Organization (WAO) suggested 2015 on their guidelines on the prevention of allergy “using probiotics in a) pregnant women at high risk for allergy in their children, b) woman who breastfeed infants at high risk of developing allergy and c) in infants at risk of developing allergies, “because considering all critical outcomes there is a net benefit resulting primary from prevention of eczema (conditional recommendation, very low quality of evidence) (14).
- The German evidence-based and consented guidelines on allergy prevention concluded 2014 that a preventive effect of probiotics and prebiotics could be shown only for atopic eczema. A recommendation regarding specific probiotic preparations, applications, duration and time point cannot be made due to the heterogeneity of the bacterial strains and study design (Evidence level 1a – 2b). With respect to prebiotics a recommendation can not be made due to the low

number and heterogeneity of studies (Evidence level 1b – 2b). (<http://www.awmf.org/leitlinien/aktuelle-leitlinien/ll-liste/deutsche-gesellschaft-fuer-allergologie-und-klinische-immunologie.html>).

In conclusion currently there is no positive recommendation for scientific societies to use pre- or probiotics for treatment of food allergy or other allergic manifestations and for prevention of food allergy, allergic rhinitis, and asthma. Discrepant recommendations exist for probiotics for prevention of eczema in high risk infants.

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