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REVIEW

Intestinal microbiota and allergic diseases: A systematic review

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Abstract Evidence suggests that possible imbalances in intestinal microbiota composition may be implicated in the occurrence of allergic diseases. Although several studies published until 2006 indicated a correlation between microbiota composition and allergic symptoms, it has not been possible to distinguish protective microorganisms from those associated with increased risk of allergic diseases. Therefore, the objective of this study was to review the studies published since 2007 that address the intestinal microbiota in allergic diseases. Twenty-one studies were identified after excluding those that performed a clinical intervention before stool collection. In the early microbiota of children who later developed allergies, lower bacterial diversity was observed, with a predominance of Firmicutes; a higher count of Bacteroidaceae; a higher prevalence of the anaerobic bacteria *Bacteroides fragilis*, *Escherichia coli*, *Clostridium difficile*, *Bifidobacterium catenulatum*, *Bifidobacterium bifidum*, and *Bifidobacterium longum*; and a lower prevalence of *Bifidobacterium adolescentis*, *B. bifidum*, and Lactobacillus. In the microbiota of allergic children whose intestinal microbiota was assessed at the onset of allergic symptoms, there was a higher count of Bacteroides; a lower count of *Akkermansia muciniphila*, *Faecalibacterium prausnitzii*, and Clostridium; a higher prevalence of *B. adolescentis*; a lower prevalence of *B. catenulatum* and *Staphylococcus aureus*; and a lower bacterial diversity.

Introduction

The intestinal microbiota is a complex ecosystem of great importance for health and is composed of both aerobic and anaerobic bacteria.[1] The gastrointestinal tract may be

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considered sterile during intrauterine life and is colonised after birth. Bacterial colonisation depends on several factors, particularly the type of childbirth, vaginal or caesarean,[2] and the method by which the child is fed during the first months of life.

Evidence suggests that possible imbalances in the composition of the intestinal microbiota and its relationship with the host may be implicated in the occurrence of allergic diseases.[3] This hypothesis has led to a number of investigations to elucidate the relationship between the composition and function of the intestinal microbiota and the onset of allergic diseases.[4]

Penders et al.[5] reviewed 18 studies on the association between the intestinal microbiota and allergic diseases. This study evaluated papers published between 1999 and 2006, primarily observational studies that compared healthy and allergic individuals. The profile of the intestinal microbiota of individuals with eczema/atopic dermatitis, food allergy, wheezing, allergic rhinitis, asthma and/or sensitisation was evaluated. The composition of the faecal microbiota was analysed using different laboratory techniques, from traditional bacterial culture to novel molecular biology techniques. Most studies indicated an association between microbiota composition and atopic symptoms and/or sensitisation. However, it has not yet been possible to distinguish protective microorganisms from those associated with increased risk of allergic diseases. The differences in the results were due to differences in the types of studies and laboratory techniques used to assess the composition of the intestinal microbiota.

In this context, this systematic study aimed to review the literature published between 2007 and 2013 that addresses the intestinal microbiota in allergic diseases.

Method

In this review, all studies published between 2007 and 2013 that compared the intestinal microbiota of allergic patients (atopic dermatitis, food allergy, wheezing, allergic rhinitis, asthma and/or atopic sensitisation) with those of healthy individuals were evaluated. Clinical trials with interventions were not included except when the composition of the intestinal microbiota on admission was evaluated before the intervention.

The studies were evaluated for sample size, place of study, age range, study design, criteria for the diagnosis of allergic diseases, and composition of the faecal microbiota.

To identify studies addressing this topic, an extensive literature search was conducted using the following databases: 1. PubMed, a database developed by the National Center for Biotechnology Information (NCBI) at the National Library of Medicine (NLM), which integrates information from NCBI databases with the PubMed database and includes MEDLINE, nucleotide sequences, protein sequences, macromolecular structures, and whole genome sequences; 2. IBECS, a database that uses the LILACS methodology and allows the selection of scientific studies on health sciences published in Spain; and 3. LILACS, a database produced by the institutions that form the Latin American and Caribbean System on Health Sciences Information. LILACS has catalogued technical–scientific data in the health sciences produced by Latin American and Caribbean authors published since 1982.[6]

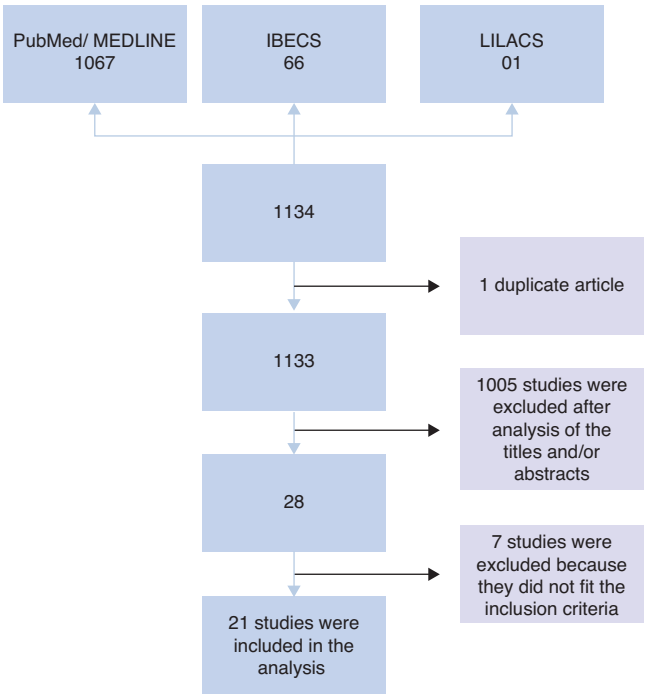

Figure 1 Study flowchart.

For the search, the following keywords and limits were used: (''Intestines'' [Mesh] OR intestin* OR gut OR gastrointestin* OR enteric) AND (flora OR microbiolog* OR microflora OR bacteria OR bacterial OR colonisation OR colonisation OR microbes OR microbial OR microbiota) AND (hypersensitivity OR atopic dermatitis OR allergic OR allergy OR atopic OR atopy OR eczema OR rhinitis OR asthma), as previously reported.[5]

Results

Initially, 1134 studies were found in PubMed, IBECS, and LILACS databases. Of these, one study was found in duplicate that was catalogued in both IBECS and LILACS. Therefore, an analysis of titles and/or abstracts of 1133 studies was performed considering the inclusion criteria. After this analysis, 1105 studies were excluded, and 28 studies remained. Of the 28 studies, seven were excluded after analysis of the full article because they did not meet the inclusion criteria; i.e., four were intervention studies that did not provide information on the microbiota at admission,[7–10] two involved children born to mothers who received probiotic intervention during gestation,[11,12] and one did not compare the microbiota of allergic and non-allergic patients.[13] Therefore, 21 articles were included in the analysis (Fig. 1).

In Tables 1 and 2, the abstracts are presented according to the period in which stool collections were performed in relation to the assessment of allergic diseases. Table 1 lists 16 studies wherein stool collection was performed before assessment of the presence of allergic diseases; and Table 2 lists five studies wherein stool collection was performed during the assessment.