Diet and food allergy development during infancy: Birth cohort study findings using prospective food diary data

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Background: After an era of only considering the allergenic properties of the infant diet and allergy outcomes, emerging data suggest that the overall composition of the infant diet might be a more important factor in the development of allergic disease.

Objective: We sought to assess the relationship between infant dietary patterns in the first year of life and development of food allergy by age 2 years.

Methods: We performed a nested, case-control, within-cohort study. Mothers kept prospective food diaries for the first year of life, with resultant diet data coded in a unique manner to produce new variables, which were then analyzed by using principal component analysis to identify infant feeding patterns within the study subjects.

Results: Principal component analysis of diet diary data from 41 infants given a diagnosis of food allergy based on results of double-blind, placebo-controlled food challenges in the first 2 years of life and their 82 age-matched control subjects provided an early infant diet pattern and an ongoing diet pattern. There was no difference between the study groups for the early infant diet pattern, but for the ongoing diet pattern, there was a significant difference between the groups ($P = .001$). This ongoing dietary pattern was characterized by higher intake of fruits, vegetables, and home-prepared foods, with control infants having a significantly higher healthy infant diet dietary pattern score than children who had a food allergy.

Conclusions: An infant diet consisting of high levels of fruits, vegetables, and home-prepared foods is associated with less food allergy by the age of 2 years. (J Allergy Clin Immunol 2014;133:511-9.)

Key words: *Food allergy, double-blind, placebo-controlled food challenge, principal component analysis, infant feeding, prospective food diary data*

There is "compelling evidence" for an increase in food allergy prevalence,[1] and it has been hypothesized that changes in diet might be responsible for this increase. The changes in dietary intake that have been suggested to have a causal link with allergy development are a decreased intake of fruits and vegetables,[2,3] a change in the types of fat in the diet,[3,4] or both. This has led to an interest in the role of specific nutrients, foods, or both in allergy development[5,6] and also the link between diet and existing allergic disease.[7-9]

The role of the infant diet in the development of food allergy has long been researched, with studies looking at the timing of important feeding events during infancy[10-13] or the diet's content of particular nutrients, such as long-chain polyunsaturated fatty acids,[14,15] vitamin D,[16-18] and folic acid.[19,20] However, a number of nutritional/dietary variables might be acting on the development of food allergy in infants, and therefore focusing on one nutrient or dietary characteristic (eg, timing of solid introduction) might be an oversimplification of the complex interactions taking place.

Looking at the pattern of consumption as opposed to focusing on individual nutrients can take into account nutrient interactions of known or unknown effects, a process thought to be particularly useful when looking at disease etiology. This type of analysis is popular and has been advocated as a valid method of looking at nutritional data.[21] It has been used to describe dietary patterns that might be affecting normal development[22] or disease outcome.[23] To date, no work looking at dietary pattern analysis in infants and allergy outcome have been published. The purpose of the present study was to use principal component analysis (PCA) on prospective food diary data to investigate whether infant feeding patterns, in particular a feeding pattern that could be described as meeting infant feeding guidelines (described in this article as a healthy infant diet),[24] are associated with the development of food allergy.

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Abbreviations used
DBPCFC: Double-blind, placebo-controlled food challenge
PCA: Principal component analysis
PIFA: Prevalence of Infant Food Allergy

METHODS

Study design

The Prevalence of Infant Food Allergy (PIFA) study is a prospective birth cohort of 1140 babies recruited between 2006 and 2008 and comprised the United Kingdom cohort of the EuroPrevall project.[25] Infants with food allergy from the PIFA study and their 2 age-matched control subjects were included in a case-control study that was nested within a cohort because analysis of prospective food diaries for all study infants was not possible within the study resources. Cases were diagnosed by means of double-blind, placebo-controlled food challenge (DBPCFC).[26] Control subjects were selected by approaching parents of infants in the cohort with birthdays just before or after the index participant until 2 control subjects were found. Control participants were assessed with the same symptomatic questionnaire and physical examination as the symptomatic infants to ensure they did not have food allergy and were not sensitized to any food.[26]

PIFA study

The PIFA study has a longitudinal prospective cohort design starting from birth. Pregnant women were recruited by one of the study researchers when informed consent was obtained and baseline information on socioeconomic, environmental, and family allergy history was collected. At this appointment, women were also invited to keep food diaries for their infants from birth until 1 year of age and were instructed how to do so. Mothers/caregivers returned the food diaries to the study office monthly. Symptom sheets were sent every 2 months to facilitate identification of symptomatic infants. In addition, parents were asked to contact the study team if they thought their child had signs of allergic disease. When each infant was 12 and 24 months of age, one of the parents was asked to complete the EuroPrevall telephone questionnaire.[26] The symptomatic sheet, telephone calls to the study office, and the 12- and 24-month questionnaires were used to identify any infant who might have a food allergy.

Food allergy diagnosis

Possible cases of food allergy were triaged by means of telephone, and those fulfilling the EuroPrevall-wide criteria for assessment were invited for an outpatient visit, where the EuroPrevall symptomatic questionnaires and skin prick tests were completed, a physical examination was undertaken, and a blood sample was taken.[26] Any infant with a convincing clinical history of food allergy, a positive specific IgE level to a common food allergen (≥0.35 kU/L), and/or a positive skin prick test response (≥3-mm wheal) was started on an exclusion diet for the suspected food or foods. If symptoms improved, the child attended the Southampton Wellcome Trust Clinical Research Facility for a DBPCFC.[26] The diagnostic criterion for food allergy in this study was a positive DBPCFC result or a convincing history of anaphylaxis.

Dietary intake data

Parents were asked to record daily anything their child ate or drank for the first year of life on specifically designed food diary sheets designed and instructed on their completion. Diary sets, made up of 4 weekly sheets, were sent out every 2 months, with parents returning each diary to the study office on completion. Freepost envelopes were provided. Parents were given no advice on how to feed their infant unless they were given a diagnosis of a food allergy. However, if they asked for advice, they were given the national feeding advice of the time, which was to exclusively breast-feed for 6 months, and not to introduce solids until this age.[27]

On receipt in the study center, the diaries were reviewed to ensure they were fit for purpose. Where they lacked adequate detail (eg, brand name of commercial baby food given), parents were contacted by telephone so that these data could be recorded.

For each week's diary, the foods/ingredients the child had eaten were coded and entered into Excel. For this, details of ingredients were obtained from the relevant food companies or from the recipe information provided by the parent/caregiver. If recipe/ingredient information was not provided, then ingredients of standard recipes from food composition tables[28] were used. The resultant Excel data file was run through an SAS program (SAS Institute, Cary, NC) written for the purpose, which converted the weekly yes/no data into new variables, such as the number of weeks an infant was breast-fed, when an infant first had a particular food/ingredient, and how many weeks in total an infant ate a food/ingredient. These new SAS variables were then imported into SPSS software (SPSS, Chicago, Ill), in which further analyses could be run.

Infants suspected of having a food allergy were started on an avoidance diet for the suspected foods. If the allergy was confirmed, the avoidance diet continued, but if the allergy was not confirmed, the food was reintroduced into the diet. No control child was given avoidance advice.

Statistical analysis

A descriptive analysis of the baseline characteristics obtained by means of a standard questionnaire administered at recruitment[26] was carried out for infants involved in the study by using SPSS version 17. PCAs were carried out on selected variables. The PCA is a mathematic way of explaining the pattern of correlations within a set of observed variables.[29] It is often used in data reduction to identify a small number of factors that explain most of the variance observed from a much larger number of variables but can also be used to generate hypotheses regarding causal relationships. The variables included in the model were selected by using (1) findings from previous infant feeding studies and (2) observations made during infant food diary coding. Because of the large difference between the early infant diet, which is predominantly milk based, and the infant diet after the introduction of solids, 2 separate PCAs were run on the intake data for the first year of life, with different variables selected for each. This maximized the potential of the prospective diary data to pinpoint any factors in the diet that might be initiators or promoters of food allergy development, something that could have been lost if the data were combined into one large pattern covering the first year of life.

The first PCA looked at characteristics of the early infant diet, such as duration and exclusivity of breast-feeding, infant formula use, and timing and types of solid food introduced into the infant diet. The second analysis looked at the diet from solid introduction to 1 year of life and was termed the ongoing infant diet. It incorporated such characteristics as type of foods eaten, use of commercial infant foods, and healthy versus unhealthy weaning foods, as defined by infant feeding guidelines.[30] Because each PCA included the appropriate variables for the characteristics of early or ongoing diet, there was no need to place *a priori* cutoffs for early and ongoing diet, which meant all the available data for each infant were captured in each PCA.

Reverse causation can be a problem in studies looking at the relationship between infant feeding and disease development and needs to be considered in analyses. There was no statistical difference in the age that egg, milk, wheat, and fish was introduced into the diet of the infants with food allergy compared with their control infants (data not shown), and therefore these foods were incorporated into the first PCA looking at the early infant diet. For the analysis looking at the ongoing infant diet and food allergy development, foods to which the infants were allergic (ie, milk, egg, and peanut) were not incorporated into the analysis to reduce the likelihood of reverse causality affecting the analysis. To identify what effect (if any) exclusion of these foods might have had on the results of the PCA, the analysis was also carried out including these allergenic foods. Each infant's score within each pattern was then saved as a new variable, and a Mann-Whitney *U* analysis was carried out to establish whether there was a difference in mean scores for the patterns between infants with food allergy and control infants. Finally, a multivariate analysis, which included variables associated with food allergy development