Texas A&M University, Nutrition 481

Optimal Infant Nutrition

Breast Feeding and the Introduction of Complimentary Foods to Prevent Food Allergy

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Background

Living with food allergies presents a unique set of problems that range from the need to carefully check ingredients to taking reactionary measures against life-threatening symptoms. People suffering with food allergies may experience rashes, gastrointestinal symptoms, swelling, wheezing and anaphylaxis, among other symptoms[1]. This condition is affecting a growing number of Americans, with the percentage of American children suffering from food allergy increasing from 3.4% to 5.1% from 1997 to 2011[2]. This rapid increase cannot simply have a genetic cause and has forced many health professionals to question whether dietary factors are responsible.

Introduction

Human milk is well-known as the epitome of the complete food for infants. For newborns and young infants, no formula can rival the comprehensiveness of mothers' milk. Breast feeding has been shown to protect against a host of conditions for the infant, including both type 1 and type 2 diabetes mellitus, childhood overweight and obesity, sepsis and diarrhea[3], and contains immune factors like secretory IgA (sIgA), cytokines, CD14 and fatty acids that aid in proper function and maturation of the infants' gastrointestinal system, as well as protecting against infection[4].

The World Health Organization currently recommends that infants be exclusively breast fed for a minimum of 6 months, with continued breast feeding once complimentary foods have been introduced for up to 2 years or longer[5]. Six months of exclusive breast feeding has been the recommendation since 2001. Although these recommendations take more into consideration than risks of food allergy, more women have chosen to

comply with these recommendations. After this recommendation was made, more women chose to exclusively breast feed their children for 6 months or longer; the prevalence of food allergies has risen during the same time period[6].

Perfect Timing

Emerging research suggests that introducing complimentary foods to infants earlier than 6 months may have protective effects against allergic disease and food allergy. Bright, et al. analyzed the intake of 994 children using information from the Finish Type 1 Diabetes Prediction and Prevention Nutrition Study. They hypothesized that the age of infants at the introduction of complimentary foods was related to allergic sensitization. Researchers collected dietary assessments at the ages of 3, 6 and 12 months, then measured for the main antibody involved in the allergic response, immunoglobulin E (IgE), at 5 years of age for the following foods: egg, cow's milk, fish, wheat, dust mites, cat, timothy grass and birch. Potatoes were the most common first food in this population and the average age of introduction of complimentary foods in this study was 3.5 months. The results of this study demonstrated that late introduction of potatoes (later than 4 months), oats (after 5.5 months), meat (after 5.5 months), rye (after 7 months), fish (later than 8.2 months) and eggs (later than 10.5 months) was associated with allergic sensitization to other allergens, not necessarily just those foods. For instance, cow's milk specific IgE was associated with delayed exposure to fish and eggs. This indicates that certain foods may initiate allergic responses at different stages of infant development, and that late exposure to some foods are correlated with allergic sensitization to similar substances in other foods. They concluded that delayed

introduction of solid foods increased the risk of allergic sensitization, instead of decreasing it as previously thought[7].

Comparable results were seen in research with wheat and peanuts. In a study from Poole, et al., researchers discovered that delayed exposure to wheat (later than 6 months) was correlated with wheat allergy, and that the protective effects of breast feeding were not seen by extending its practice beyond 6 months. This study followed 1612 children for an average of 4.7 years, using interviews to collect allergy and dietary information at 3, 6, 9, 12 and 15 months, then annually after that. Interviewers asked parents of the children enrolled in the study about the presence of allergy to wheat, cow's milk or dairy, infant formula, nuts, eggs, shellfish or other allergies (food and non-food). Parents were also asked to describe the timing and introduction of all foods consumed by their children in the 3 months since their last interview, including human milk and complimentary foods. Sixteen (0.99%) of these children reported wheat allergy and four tested positively for wheat-specific IgE[8]; this is more than double the incidence of wheat allergy in the population at large, which averages about 0.4%[9]. Among the 16 children who reported wheat allergy, 12 (75%) were introduced to wheat at or after 7 months old. Each of the four children in which wheat-specific IgE were detected were first introduced to wheat after 6 months of age. Authors of this study suggest that there appears to be an ideal window of opportunity for introducing complimentary foods for prevention of food allergy. Offering complimentary foods during this time exposes the infant to new substances while he or she is still consuming small amounts of these foods, but at a time when the mucosal immune system is fully developed[8].

Both of these studies use information collected from populations with the HLA-genotype that were screened for type 1 diabetes risk factors, possibly limiting the scope of application for each. The population at large may have different responses to breast feeding and timing of complimentary foods. Though efforts were made to account for confounding variables, each of these studies was a prospective cohort study and subject to recall bias and reverse causation[7,8]. However, randomized control trials with breast feeding practices are unethical; therefore, this format may be the most effective method of studying feeding practices in human infants. Identifying a consistent definition of food allergy was another weakness in these studies. Bright et al. used measures for IgE-mediated allergic responses and sensitizations[7], while Poole et al. used both IgE concentrations and occurrence of symptoms with or without a physician's diagnosis[8]. While IgE concentrations offer a tangible measure of allergic sensitization, they do not account for the cell-mediated or non-IgE allergic response[10].

Common Weaning Foods

Foods that are commonly used to wean infants vary by culture. Within these cultures, prevalence of allergic reactions to these foods is low, indicating that there is either a genetic predisposition to tolerance of these foods or that frequent exposure during the weaning process develops tolerance in these infants. Toit, et al. developed a study to address this 'nature versus nurture' dispute surrounding weaning foods common in different cultures. Israeli Jewish children are frequently weaned on peanuts, a common allergen in western culture that can result in deadly symptoms. This study observes the difference between Jewish children in Israel, who consume an average of 7.1g of peanut protein per month during their first year, and Jewish children living in the UK who

consume an average of 0g of peanut protein per month in their first year. The rate of allergy to peanut is 10-fold higher in the Jewish children living in the UK versus the population living in Israel, which is exposed to peanut protein at a much younger age and at a greater amount. Though there are likely a vast number of genetic variations within these populations, compared to the genetic diversity seen in many societies, these populations are relatively homogenous and share many common dietary practices[11].

Data for this study was collected via food frequency questionnaires and food allergy questionnaires, with food allergy defined as experiencing common allergy symptoms within 2 hours of ingesting the food. Those with self-identified food allergy were then tested for elevated IgE levels and positive results from a skin prick test[11]. This methodology was likely more effective at assessing allergic sensitization than previous studies discussed due to the specificity of their definitions and the inclusiveness of using both IgE testing and skin prick testing; conversely food frequency questionnaires do lend themselves to recall bias.

Figure 1

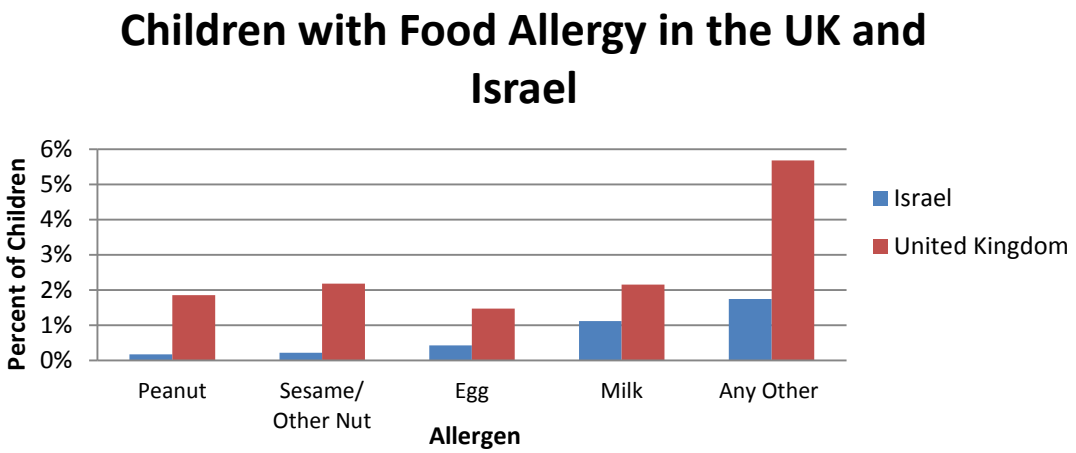

Figure 1: The percentage of peanut and all other food allergies accounted for was much lower in populations where peanuts were introduced earlier and in much higher amounts.

Adapted from reference 10.

After adjusting for variables such as socioeconomic status, age, and the presence of other food allergies, the risk for peanut allergy was much higher in the Jewish children living in the UK compared with those living in Israel, as was the risk for all other food allergies accounted for in this study (Figure 1). Even when focusing only on those children with high risk for peanut allergy (i.e. those with eczema), the occurrence of peanut allergy was found to be 6.46% in the UK and only 0.79% in Israel. Surprisingly, the duration of breast feeding, including exclusive breast feeding was longer in the UK than in Israel, suggesting that beyond a certain stage of development, breast feeding may not protect against food allergy[11].

Genetic Susceptibility

Those who suffer from food allergies are shown to have a genetic predisposition, with opportunistic environmental exposure. Physiological conditions that may predispose an infant to food allergy are a leaky intestinal barrier, immature sIgA systems, and a high gastric pH. These conditions can lead to activation of mucosal immune responses,

rather than suppressing them, which is the normal response[12]. Hong, et al., produced a recent study with the aim of determining if children with certain genotypes experienced preventing or promoting effects of breast feeding in regard to allergic sensitization. An ethnically diverse group that included 970 children from the Boston Birth Cohort and their mothers was studied for up to 6 years as part of the children's pediatric primary care appointments. During these visits, blood samples were collected (for IgE concentrations and for genotyping), and information was gathered on breast feeding, maternal allergy, and each child's allergic status. Breast feeding information was collected at age 6 months and was categorized as either "exclusive breast feeding" or "ever breast feeding," which included the use of formula and complimentary foods. The duration of exclusive breast feeding or introduction of solid foods was recorded for both sets of breast feeding mothers[13].

The collected information was compared to the blood samples. Genetic variations of 18 different genes were recorded as were the children's responses to breast feeding in relation to food sensitization. Within each gene, select single nucleotide polymorphisms (SNPs) were chosen for a total of 98 SNPs. These polymorphisms were selected based on their function within the gene (they had to be coding SNPs), the placement of the SNP (creating or disrupting a splicing site) and the prevalence of the SNP in the population at large (allele frequency of greater than or equal to 0.05). These SNPs were also thought to be functional variants as defined by bioinformatics tools.

Of the children observed, those who were ever breast fed had a higher prevalence of food sensitization than those who had never been breast fed. When genotype was considered, those children with the rs425648 GG genotype were more likely to suffer

from food allergy if they were ever breast fed, but those with the rs425648 GT/TT genotype had a reduced the risk of food allergy with breast feeding. This particular SNP is responsible for products involved in the T_H1 response[13], which is active in cell-mediated immunity, as well as inflammation due to phagocytic action[14]. Many other genes were found to have similar results on food sensitization in breast fed or non-breast fed children; the promoting or preventing effect of breast feeding in regards to food sensitization depended on the genotype of the individual (figure 2). This study also found that if the children had more than one gene that was unfavorable to breast feeding, the likelihood that they would display food sensitization was much stronger[13].

Figure 2

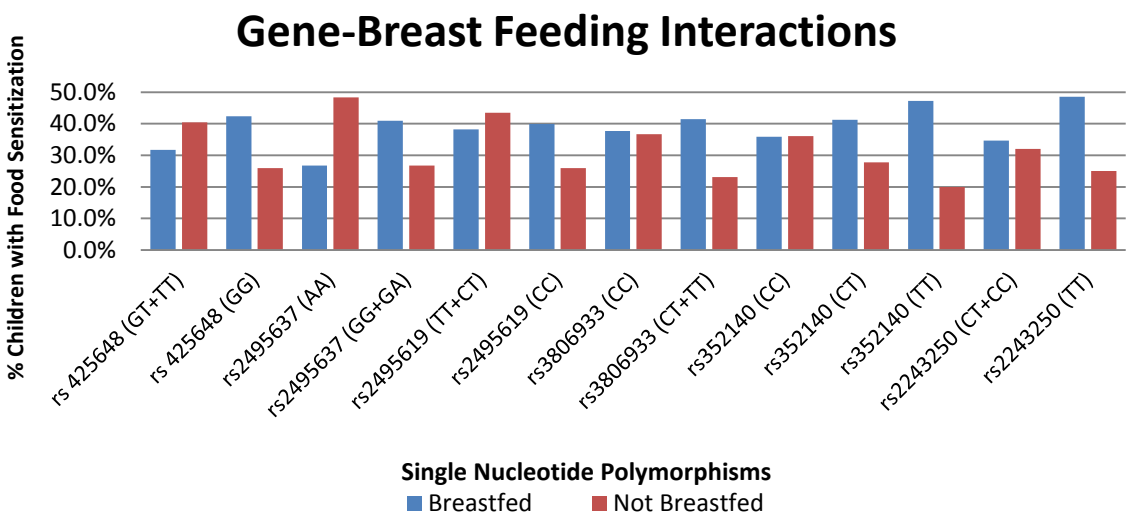

Figure 2: Genetics was found to play an important role in whether or not breast feeding played a role in inhibiting or promoting food sensitization, as seen in the varying prevalence of food sensitization seen for each genotype.

Adapted from reference 12.

The study from Hong, et al. accounted for many confounding variables, such as maternal age and smoking status, parental history of allergy and household income;

however, its cohort was susceptible to reverse causation. To prevent this, they controlled for early signs of allergy and ensured that this did not influence the decisions of the parents to breast feed or not to breast feed their children. The study also used an ethnically diverse population, but, with more than half of the participants being African American, it was not a population that proportionately resembles that of the United States. Since the results were so dependent on genotype, it must be taken into consideration that the SNPs used could be more or less prevalent in the African American population than in the United States at large, possibly affecting the ratios of people affected[13].

The previous study indicated where the genetic link between breast feeding and allergy may lie in the infant, but research from Duchén, et al. reveals that there may be a genetic component affecting the composition of mothers' milk as well. In their recent study, they sought to explain the controversy over the protective or promoting effects of breast feeding on food allergy by analyzing the composition of milk of 160 mothers with and without atopy or allergy and who's children were classified as having atopy or allergy. The authors specifically reviewed the concentration of long chain polyunsaturated fatty acids (PUFA) and sIgA[15], an antimicrobial and anti-inflammatory antibody found in human milk[16]. This research differentiated between atopic and allergic participants, with atopic being defined as those with a positive skin prick test and allergic participants as those who self-identified with non-specific symptoms of allergic disease. After researchers controlled for confounding variables such as smoking habits, exposure to pets, birth weight and timing of introduction of foods like milk and egg, It was discovered that, though sIgA concentrations had no correlation with atopy or allergy

in either the mother or child, mature milk (sampled at 1 and 3 months post-partum) from mothers with atopic children had an increased ratio of n-6 : n-3 PUFA than milk from mothers with children not suffering from atopy, and that atopic mothers tended to have low levels of linoleic acid, α-linoleic acid, n-6 long chain PUFA, and n-3 long chain PUFA in their early transitional milk (figure 3). Varying amounts of these fatty acids could affect the activation or suppression of the immunes system due to their individual relationships with inflammatory reactions in the body[15].

Figure 3

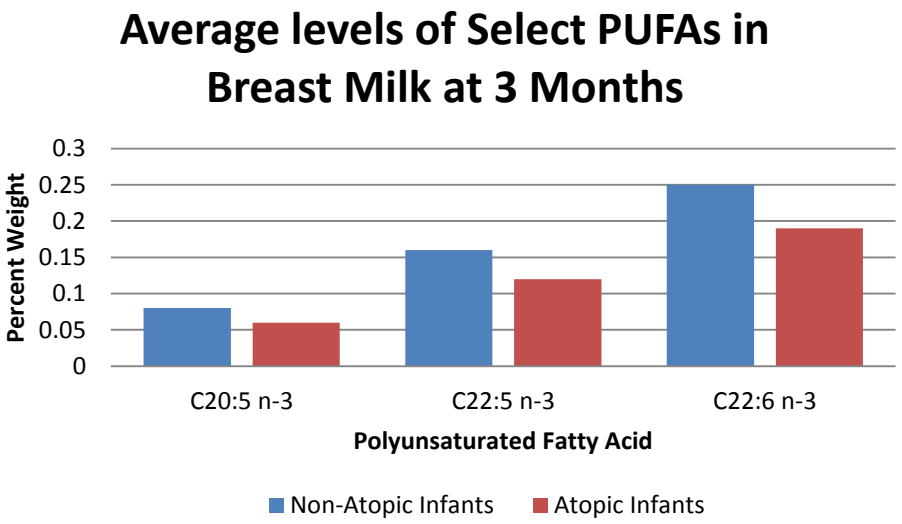

Figure 3: Infants of mothers with lower levels of the n-3 fatty acids in their milk were shown to be more likely to suffer from atopic disease. Levels of fatty acids were measured by weight in the sample and are shown as a percentage of the sample weight.

Adapted from reference 14.

The authors of this study hypothesized that this difference is likely due to the way fatty acids were metabolized in atopic and non-atopic mothers, linking the difference to an enzyme called δ-6-desaturase that desaturates linoleic acid to γ-linoleic acid and is essential to the elongation of other PUFA. The proper function of this enzyme could be a reason that the composition of milk varies among mothers with and without atopy. Many of the studies seeing various results when analyzing the effects of breast milk on

the likelihood of allergy and atopy could be observing differences in the individual's metabolism and subsequently, their milk.

The strengths of this study were well defined classifications of atopy and allergy, as well as the use of blood samples and skin prick tests for verification of allergic status. Researchers in this study also made sure to control for confounding variables such as maternal diet, using a 24-hour recall, however their population was small and concentrated to women delivering their infants in Linköping, Sweden, possibly reducing the applicability of the results to other populations[15].

Conclusion

Each of these studies supports the hypothesis of exposure, not avoidance to prevent food allergy. Though genetic components clearly play an active part in the development of food allergy, length and exclusiveness of breast feeding, timing of introduction of complimentary foods and repeated exposure to a variety of foods appear to reduce the occurrence of food allergy and sensitization. It seems as if the WHO's recommendations to exclusively breast feed for 6 months or longer may be contributing to the growing number of children suffering from food allergies in developed countries, and that apart from sequencing each mother's and newborn's genome, a strategic weaning plan that includes knowledge of when to introduce which foods may be the most beneficial method of preventing food allergies.

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