

THE ROLE OF BREASTFEEDING AND WEANING PRACTICES IN ALLERGIC DISEASE DEVELOPMENT

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ABSTRACT

Data from many studies demonstrate that allergy prevalence has been on the increase in the past few decades. This alarming burden of allergic disease highlights the importance of the development of primary prevention strategies. Breastfeeding is well known for its beneficial short- and long-term effects on a variety of health outcomes. However, there is still no agreement on the protective role of breastfeeding in relation to allergic sensitisation and disease development. Exclusive breastfeeding for six months is recommended but it is unclear whether a unified approach should be used in all children or if weaning should be initiated earlier in infants with a high risk for allergy development. The timing of solid food introduction is currently a matter of discussion, with emerging evidence suggesting the potential benefits of the early introduction of 'highly allergenic foods'. This review summarises the evidence about breastfeeding and food introduction in infancy and their association with the development of allergic disease later in life.

INTRODUCTION

In the past few decades, the prevalence of allergic disease has been on the increase worldwide.¹ This is particularly evident in Westernised and urbanised countries,² but recent data suggest that it is also becoming an emerging problem in Africa.³ 'The Hygiene Hypothesis' has been proposed initially as the main theory purporting to explain the increase in the prevalence of allergic disease.⁴ This points to the impact of modern living, which has resulted in the reduced stimulation of the immune system by microbial antigens and a concomitant reduction in the repertoire of specific IgM and IgG to different organisms. It highlights an inverse relationship between the risk of atopic disease (known to be associated with a Th2 immunological response) and the lack of early-life exposure to bacteria (promoting a Th1 response). This 'lack of exposure' includes factors such as later birth order and/or number of siblings, early attendance at daycare and early exposure to pets.⁵ Recent research by Sozanska and colleagues provides further data in support of the 'hygiene hypothesis', which shows an association between environmental influences and allergy development.⁶ The authors report an increase in the prevalence of atopic diseases over an eight-year

period in a Polish population, which can be explained by a reduction in contact with domestic animals and a reduction in unpasteurised milk consumption, due to their accession to the European Union.

There are, however, other components of the modern world environment and lifestyle which may explain a steady increase in allergy. These include nutritional changes such as reduced fresh fruit intake, deficits of omega-3 and omega-6 polyunsaturated fatty acids (PUFAs), which are related to a reduced fresh fish intake, vitamin D deficiency (due to lack of sunlight exposure) and other environmental factors. The increased incidence and prevalence of allergic disease has lately been recognised as having reached pandemic proportions, highlighting an increasing need for an effective primary prevention strategy.⁷

Primary allergy prevention is an important measure aimed at reducing the risk of allergic disease.^{8,9} Preventive strategies are of particular importance for children with a family history of allergy because they are at a higher risk of allergy development,^{10,11} especially if the mother or both

parents are allergic.¹² Existing evidence suggests that the 'window of opportunity' for allergy prevention is located between the last trimester of pregnancy and six months postpartum.^{7,13,14} During the last stages of pregnancy, interventions in the maternal diet were associated with subsequent allergy development in children;¹⁵ similar trends were seen in interventions in breastfeeding patterns and/or the timing of solid food introduction.^{16,17} This overview article is aimed at critically appraising the existing evidence concerning breastfeeding and weaning practices in the light of allergic disease development.

BREAST MILK AND BREASTFEEDING EFFECTS

Breast milk is the primary source of nutrition for a newborn infant, and it assists greatly with the newborn's adaption to the new hostile environment. Apart from supplying major constituents such as proteins, fatty acids, carbohydrates, minerals and vitamins,¹⁸ breast milk also provides biologically active factors¹⁸ and is able to influence the maturation of an infant's gut immunity and the moderation of gut microflora. It therefore influences the baby's physical and neurocognitive development.

A significant amount of work has been done to investigate the influence of breastfeeding on child health. It is well established that breastfeeding results in many short-term benefits for a child's health (by reducing mortality and morbidity from infectious diseases) as well as the longer-term advantages (such as reducing the risk of type 2 diabetes and hypertension and increasing the IQ in adulthood).^{19,20} According to the World Health Organisation (WHO) report on the evidence about the long-term effects for infants who were exclusively breastfed for six months, such infants had lower morbidity from gastrointestinal and allergic diseases in comparison to non-breastfed children.²¹ Based mainly on these data, both WHO and the United Nations International Children's Emergency Fund (UNICEF) developed recommendations which suggested that every infant be exclusively breastfed for the first six months of life.²² More than a decade later, Kramer and Kakuma²³ performed a systematic review to assess the importance of breastfeeding duration, which partially supported the existing WHO recommendations. An analysis of more recent literature shows an association between exclusive breastfeeding for six months and a reduced risk of the development of gastrointestinal infection, an accelerated maternal weight loss after birth, and more prolonged lactational amenorrhea, but without any long-term impact on allergic disease development, growth, obesity or the cognitive ability or behaviour in the child.

The reasons behind the differences in the protective capabilities of breastfeeding remain unclear; however, some evidence suggests that they may be explained by individual variations in breast milk composition. A number of studies have shown significant differences in the levels of

immunologically active molecules and/or polyunsaturated fatty acids in breast milk, which are related to the country of maternal origin and/or residence and maternal dietary patterns, extensive physical activity, exposure to smoking, or farming environments.^{24–44} It is still unclear to what degree the concentration of immune-active molecules in breast milk affects infant health outcomes, but a number of clinical trials have provided evidence in support of this association.⁴⁵ So far, no studies have attempted to combine detailed data on breastfeeding patterns with comprehensive breast milk compositional analysis in a large prospective cohort; this should be addressed in future research.

BREASTFEEDING AND ALLERGIC DISEASES

Although the short- and long-term benefits of breastfeeding are apparent, there is still conflicting evidence of the protective role breastfeeding plays in allergic sensitisation and allergic disease.⁴⁶ Many studies that aimed at evaluating an association between breastfeeding and allergy development have had mixed results. The outcomes vary from demonstrating the protective effects of breastfeeding⁴⁷ to showing that breastfeeding increases the risk of allergy,⁴⁸ or even exhibiting no significant effect.⁴⁹ These conflicting results highlight the need for a critical evaluation and presentation of the most current data.

The first attempt at systematically reviewing the existing evidence of breastfeeding's ability to prevent allergy development was made by Gdalevich and Mimouni in 2001 and it resulted in two meta-analyses. The first focused on the association between breastfeeding and eczema development in children⁵⁰ and the second examined the protective effect of breastfeeding on asthma prevention.⁵¹ Since then, a number of systematic reviews have been produced, with the most recent meta-analysis being by Lodge et al;⁴⁶ this provided probably the most detailed and comprehensive analyses of the current evidence. The main findings of the meta-analyses on each allergic condition are discussed below.

ECZEMA

In their meta-analysis Gdalevich and Mimouni⁵⁰ suggest the protective properties of exclusive breastfeeding on the prevention of eczema development (OR = 0.68, 95% CI 0.52–0.88), with the protective effect being particularly prominent in children with a family history of atopy (OR = 0.58, 95% CI 0.41–0.92). The outcomes of the two subsequent meta-analyses, in contrast, did not support the previous findings, and showed no protective effect from exclusive breastfeeding on eczema either in the general population (OR = 0.89, 95% CI 0.76–1.04),⁵² (OR = 0.95, 95% CI 0.85–1.07) or in children with a family history of allergy (OR = 0.78, 95% CI 0.58–1.05).⁵² Lodge and the co-authors reported a reduced risk (OR = 0.74, 95% CI 0.57–0.97) of eczema development in children below two years of age who were exclusively breastfed for more than

three to four months;⁴⁶ however, the authors admitted a risk of bias, as smaller studies showed a stronger protective effect.

FOOD ALLERGY

There are conflicting data concerning the relationship between breastfeeding and food allergy, with some cohort studies reporting a reduced risk of food allergy development in the general population^{53,54} and in high-risk children,⁵⁵ whereas other studies found an increased risk.^{56,57} The only meta-analysis to investigate this relationship – by Lodge et al – found no evidence of the protective effect of breastfeeding in preventing food allergy development (OR = 1.02, 95% CI 0.88–1.18).⁴⁶ Despite this failure to find an association between breastfeeding and reduced rates of food allergy, it is too premature to draw definitive conclusions about it, as the risk of bias and major differences in the outcome definitions in the current studies may be responsible for the inconclusive results.⁴⁶

ALLERGIC RHINITIS

Two meta-analyses systematically reviewed an association between breastfeeding and the development of allergic rhinitis, with the cumulative evidence suggesting a weak protective effect ((OR = 0.74, 95% CI 0.54–1.01),⁵⁸ (OR = 0.79, 95% CI 0.63–0.98)⁴⁶). The main limitation of the studies on this subject was the lack of prospective trials – with only one having been reported.⁵⁹

ASTHMA

Gdalevich and Mimouni reported a protective effect of breastfeeding on preventing the development of asthma (OR = 0.70, 95% CI 0.60–0.81)⁵¹ which was later supported by the results of two subsequent meta-analyses ((OR = 0.78, 95% CI 0.74–0.84)⁶⁰ and (OR = 0.88, 95% CI 0.82–0.95)⁴⁶). There is agreement that greater protective effects of breastfeeding on asthma are increasingly evident in the more recent studies, which may be explained by an improved methodology.^{46,60}

The outcomes of the meta-analyses have led to a general belief that breastfeeding can prevent allergic disease development, but they have elucidated several methodological issues that may partly explain the discrepancies between outcomes such as characteristics of and cultural approaches to breastfeeding, duration of breastfeeding, time of solid food introduction and major differences in allergic disease outcome definitions.

Existing data suggest that there is some evidence that breastfeeding and/or its duration can reduce the risk of allergic disease developing in children. However, the heterogeneity between the studies and the risk of bias do not allow us to draw definitive conclusions at this time. The protective effect for preventing eczema, allergic rhinitis and asthma seems to be greater in early life.⁴⁶

DIET DURING LACTATION AND ALLERGY DEVELOPMENT

A number of studies have evaluated the influence of maternal dietary changes during pregnancy,⁶¹ lactation⁶² or both on allergic disease development. As food allergy often develops in early infancy it was thought that there is a direct relationship between maternal diet and subsequent allergy development. It has been clearly demonstrated in human studies that food proteins pass to the baby via breast milk,^{63,64} so that the breastfed infant is exposed to food antigens in the milk, which may lead to allergic sensitisation or, alternatively, to the development of tolerance. Attempts to tackle allergy development by excluding major allergens from the maternal diet^{62,63} have largely failed, with studies producing conflicting results. Recently, Kramer and Kakuma systematically reviewed the data available from human cohorts and failed to find an association between food antigen restriction during lactation and allergy development in the child.⁶⁶ At present, there is not enough evidence to support maternal diet restriction as an allergy-prevention strategy.

- Exclusive breastfeeding for the first six months is recommended by WHO as it leads to evidence-based short- and long-term benefits for the child and the mother.
- Exclusive breastfeeding is recommended as it may reduce the risk of eczema development (in children younger than two years of age), allergic rhinitis and asthma, although the existing evidence is weak.
- The exclusion of 'highly allergenic' foods from a lactating woman's diet should not be recommended as an allergy-prevention measure.

INTRODUCTION OF COMPLEMENTARY FOODS AND ALLERGY PREVENTION

Complementary food introduction is an important step in the life of a developing infant, as the delayed or premature introduction may lead to adverse health consequences, such as food allergy development. The ideal time for introducing complementary foods remains unclear. Guidelines and recommendation documents vary between countries and professional bodies, which leads to substantial confusion among both clinicians and the public. While WHO is very clear in recommending exclusive breastfeeding for the first six months of life,²² physicians in many countries suggest complementary food introduction between four and six months. Their recommendation is driven by local policies or international societies.⁶⁷ The European Society for Paediatric Gastroenterology, Hepatology and Nutrition's (ESPGHAN) Committee on Nutrition provides a more precise timeframe of 17–26 weeks, stating that exclusive or full breastfeeding for the period of six months is still 'a desirable goal'.⁶⁸

It was thought for a long time that the intake of 'highly allergenic' food during lactation as well as its introduction into the babies' diet should be delayed as doing so decreases the risk of allergy development. Experts also recommended the strict avoidance in high-risk infants of

dairy products until one year of age, eggs until two years, and peanuts, nuts and fish until three years of age.⁶⁹ Despite these efforts and the strong emphasis on the avoidance of highly allergenic foods, the prevalence of food allergy has been increasing. This trend has raised the question of the effectiveness of this approach.

A recent systematic review of the available evidence has shown that avoidance strategies in early infancy have had little effect on food-allergy development.⁷⁰

Many studies have looked at the relationship between infant diet in the first year of life and allergy development. Animal⁷¹ and later human⁷² data have suggested that consistent exposure to an allergen may drive the development of oral tolerance. Du Toit and colleagues have studied Ashkenazi Jewish children residing in the United Kingdom and Israel in a large cross-sectional study.¹⁶ They found a significant difference in the prevalence of peanut allergy between the two groups. This was related to earlier peanut introduction into the infant diet in Israel due to local habits and much larger quantities of peanut being eaten by the children. Similar trends were seen in the later studies assessing egg introduction.^{73,74} The outcomes of two large randomised controlled trials published in the past two years^{17,75} has provided more data suggesting that targeted food introduction may be beneficial to the developing child. The first study demonstrated a significant reduction in the prevalence of peanut allergy in children at high risk of allergy development who had been consuming peanuts regularly between four and 11 months of age.¹⁷ The second trial looked at early food introduction (from three months of age) and concluded that it may decrease the risk of food-allergy development.⁷⁵ The authors reported significantly lower relative risks of peanut and egg allergy in the early-introduction group, with no difference in the prevalence of milk, sesame, fish or wheat allergy.

At present, an apparent shift in expert opinion is seen, trending towards the early introduction of certain highly allergenic foods. This is driven by the emerging data showing that the early introduction of at least some of highly allergenic foods will be beneficial to the baby.⁷ In January 2017, the American National Institute of Allergy and Infectious Diseases (NIAID) updated its guidelines on peanut allergy prevention,⁷⁶ recommending that peanut-

containing foods should be introduced between four and six months of age in egg-allergic infants and/or babies with severe eczema and at six months of age for infants with mild to moderate eczema. They also suggested that infants with no food allergy and/or eczema may safely have peanut-containing food as a part of their diet alongside other solid foods.

- There is no evidence that the delay in introducing highly allergenic foods is an effective measure for preventing primary allergy.
- There is emerging evidence that the earlier introduction of highly allergenic foods into an infant's diet may reduce the risk of food-allergy development, at least for some foods (e.g. peanut).

CONCLUSION

The increase in the prevalence of allergic disease in children and adults draws more professional attention to their early life events. In recent years, several allergy-prevention measures have been developed and tested, with mixed results. It becomes more evident that the period between the last trimester of pregnancy and six months of age is the perfect time for implementing intervention strategies. The obvious candidate – breastfeeding – confers short- and long-term benefits on the infant, but it is still unclear whether it reduces the risk of allergy development. This may be related to the individual variations in the composition of breast milk between women. In order to address this question fully, future research should combine data on breastfeeding patterns and duration and on the composition of breast milk.

Furthermore, the timing of food introduction is extremely important as it may lead to tolerance development, or early sensitisation. There is still no agreement on the timing of the introduction of 'highly allergenic foods', but emerging evidence suggests that at least some foods should be introduced below six months of age, especially in high-risk group infants. Further large prospective trials are required to confirm the impact of the early introduction of highly allergenic food on allergic disease development.

DECLARATION OF CONFLICT OF INTEREST

The author declares no conflict of interest.

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