

Is breast feeding a risk factor for eczema during the first year of life?

Sariachvili M, Droste J, Dom S, Wieringa M, Vellinga A, Hagendorens M, Bridts C, Stevens W, Van Sprundel M, Desager K, Weyler J.
Is breast feeding a risk factor for eczema during the first year of life?
Pediatr Allergy Immunol 2007.

© 2007 The Authors

Journal compilation © 2007 Blackwell Munksgaard

Breast feeding (BF) provides many advantages to the offspring; however, at present there is an ongoing debate as to whether or not it prevents allergic diseases. The aim of the current study was to investigate the effect of duration of BF on eczema in the first year of life. A birth cohort of 1128 infants was followed prospectively from 5 months of pregnancy. Data were collected using questionnaires, a medical examination and blood tests for allergy at the age of 1 yr. Breast feeding was not statistically significant associated with eczema in the first year of life [adj ORs with 95% CIs: 0.8 (0.4–1.3), 0.8 (0.5–1.3) and 1.0 (0.6–1.5) for BF duration of 1–6 wk, 7–12 wk and ≥ 13 wk, respectively]. Eczema was positively associated with atopy and educational level of the mother, use of antibiotics in pregnancy and passive smoking by the child during the first 12 months. Regular postnatal contact of the infants with dogs was inversely associated with eczema. Breast feeding was positively associated with eczema among children with non-atopic parents [adj ORs with 95% CIs: 2.1 (0.4–10.6), 2.2 (0.4–11.3) and 1.9 (0.4–8.5) for BF duration of 1–6 wk, 7–12 wk and ≥ 13 wk, respectively], whereas an inverse association was found among children with atopic parents [adj ORs with 95% CIs: 0.6 (0.3–1.3), 0.7 (0.3–1.4) and 0.9 (0.5–1.7) for the same BF durations]. However, these associations were not statistically significant. Breast feeding has no significant effect on the prevalence of eczema in the first year of life. The effect of BF on eczema in children depends on parental atopy.

Manana Sariachvili¹, Jos Droste¹, Sandra Dom¹, Marjan Wieringa², Akke Vellinga¹, Margo Hagendorens^{3,4}, Chris Bridts³, Wim Stevens³, Marc Van Sprundel¹, Kristine Desager⁴ and Joost Weyler¹

¹Department of Epidemiology and Community Medicine, University of Antwerp, Antwerp, Belgium,

²Department of Otorhinolaryngology, Head and Neck Surgery, Erasmus MC, Rotterdam, the Netherlands,

³Department of Immunology, University of Antwerp, Antwerp, Belgium, ⁴Department of Paediatrics, University of Antwerp, Antwerp, Belgium

Key words: breast feeding; eczema; childhood; allergy

Manana Sariachvili MD, Department of Epidemiology and Community Medicine, Antwerp University, Universiteitsplein 1, 2610 Wilrijk, Belgium

Tel.: 00 323 820 2992

Fax: 00 323 820 2640

E-mail: manana.sariachvili@ua.ac.be

Accepted 13 January 2007

Breast feeding (BF) has undisputed advantages over formula feeding, as it provides optimal nutrition, protects against infections, enhances mother–infant bonding, and may improve cognitive functions of the offspring (1). Breast feeding may also help prevent childhood overweight (2). Recently, it was demonstrated that BF provides long-term benefits to the risk of atherosclerosis (3).

As Grilée and Sanford reported a sevenfold increase in the prevalence of eczema in cow's milk-fed compared with breast-fed children in 1936 (4), BF has also been widely encouraged to reduce the risk of allergic disorders; however, evidence for this effect is conflicting. Some

investigators report a protective effect of BF (5–9), whereas others suggest an increased risk for the development of allergy and asthma (10–13).

The reasons for these inconsistent or even contradictory results between studies mainly relate to the use of exclusive vs. partial BF, different cut-off points for BF duration, different duration of follow-up and the ages at which outcomes are assessed. Different confounding factors and inadequate definition of outcomes may also be relevant. Furthermore, methodological problems, such as selection of study population and recall bias with respect to feeding history may produce differential bias.

In addition, according to some investigators the effect of BF on the development of allergic disorders in children seems to depend on parental atopy (14–17). Several studies show differences in fatty acids (FA) composition between breast milk from atopic and non-atopic mothers which could in part explain the disagreement between studies regarding the effect of BF on allergy (18–22). Therefore, analyses ignoring this potential interaction may lead to conflicting results, depending on the study population mix.

The aim of the present study was to examine the effect of duration of BF on the prevalence of eczema in the first year of life, taking into account other influential factors, including parental atopy.

Methods

Study population

The PIPO-project (Prospective study on the Influence of Perinatal factors on the Occurrence of asthma and allergies) started in 1997 in Antwerp, Belgium, using a cohort of children who were followed from the mother's fifth month of pregnancy. Two thousand pregnant women were approached through four gynaecologists between June 1997 and October 2001. Of these, approximately 55% were willing to participate in our study, resulting in a total study population of 1128 children. Data were collected through postal questionnaires and two home visits. At the age of 1 yr the children and their parents visited the study centre for a medical examination and a blood sample for allergy testing. At the present time the children are still in follow-up.

The Committee for Medical Ethics of Antwerp University granted approval for the assessments. The parents of the participants gave their written (informed) consent before each assessment.

Questionnaire

Detailed data on environmental factors, nutrition, use of medication during pregnancy, work situation of the mother 3 months after birth and on family history of allergy were collected from questionnaires completed by study nurses during home visits at 5 months pregnancy and 3 months after birth. Information on parental education, child's morbidity, use of medication, environment and nutrition during the first year of life was obtained from parental postal questionnaires when the children were 6 and 12 months-of-age. A combination of questions was used to define

eczema. When the children were 3, 6 and 12 months-of-age the parents were asked: 'has your child ever had an itching skin disease?', 'if yes, was this eczema?' and 'where was this localised?' As a result, eczema was defined by a parent-reported history of an itchy rash in the past 12 months with a typical distribution (neck, knee or elbow folds, front of ankles, wrists/hands or face).

At 3, 6 and 12 months parents were asked whether their child ever had been breast-fed, and if yes, whether the child was currently being breast-fed. If not, parents were asked how old (in wk) their child was when the last breastfeed was given.

Atopy status

The atopy status of the parents was assessed by measurement of specific immunoglobulin E (IgE) antibodies to seven common inhalant allergens (*Dermatophagoides pteronyssinus*, cat, dog, timothy grass pollen, mugwort pollen, birch pollen and *Cladosporium herbarum*) using a fluorescence enzyme immunoassay technique (CAP FEIA systems, Pharmacia Diagnostics, Brussels, Belgium). Children were tested on specific IgE antibodies to *D. pteronyssinus*, cat, dog, egg white and cow's milk. All analyses were performed by the Immunology Laboratory of the Antwerp University Hospital. Specific IgE levels equal to or higher than 0.35 kU/l were regarded as positive. Children were considered atopic if they had at least one positive specific IgE and were considered to have a positive family history of atopy if at least one parent had one or more positive specific IgE antibodies.

Data analysis

In univariate analyses, differences between subgroups were assessed by Pearson's chi-square test or Fisher's exact test, when appropriate, and presented as crude odds ratio (OR) with 95% confidence intervals (CI). All tests were two-sided and a p-value ≤ 0.05 was considered to be statistically significant. Multiple logistic regression analyses were used to adjust for potential confounders and the results were expressed as adjusted odds ratio (adj OR) with 95% CIs. In order to reduce the number of co-variables, a stepwise backward procedure was performed, using the Likelihood Ratio statistic ($p = 0.10$) for removal of co-variables from the regression model.

Based on preliminary analyses, BF duration was represented in the analyses as a categorical

variable (ever/never and never/1–6 wk, 7–12 wk and ≥ 13 wk). Children born before 37 wk of gestation were defined as premature. Birth weight was represented by a dichotomous variable with a cut-off point at 2.5 kg (based on preliminary analyses). Educational level was represented by a dichotomous variable, differentiating between mothers with a higher educational level (bachelor's or master's degree) and a lower educational level (secondary school or less). Prenatal use of antibiotics was considered positive when one or more courses were used during pregnancy. Postnatal use of antibiotics was considered positive when more than two courses were received during the first year of life. Maternal age was represented by a categorical variable with a cut-off point at 25 yr-of-age. Day care attendance was represented by a dichotomous variable, differentiating between study subjects attending day care (with two or more children) during the first year of life, and others. Exposure to pets was defined as regular contact at least once a week.

Statistical analysis was performed using SPSS for Windows V11.0 (SPSS, Chicago, IL, USA).

Results

Study population

A total of 1128 children were recruited into the PIPO study. Of these, 976 (87%) subjects with complete data on duration of BF during the first year were included in the current analyses. No differences in clinical outcome, parental atopy and environmental factors were found between children with a reported duration of BF and those without (data not shown).

General characteristics of our study population are shown in Table 1. Of 976 eligible infants, 725 (74%) were ever breast-fed, whereas only 236 (24%) were exclusively breast-fed during the first 3 months after birth. Mothers with a higher educational level and non-working mothers at 3 months after birth more often chose for BF. Moreover, first-born and full-term infants were more often breast-fed (data not shown).

Blood tests for total and specific IgEs were carried out at the age of 1 yr in 740 children, 555 fathers and 727 mothers. The prevalences of at least one positive specific IgE (atopy) were 13.0%, 46.3% and 40.9% for infants, fathers and mothers, respectively.

Of 976 infants in our study, 78 (8%) were born preterm (≤ 37 wk), 47 baby's (4.8%) had low birth weight (< 2500 g) and three (0.3%) had very low birth weight (< 1500 g).

Table 1. General characteristics of study population (N = 976)

Characteristic	Number	%
Gender (N = 976, boys)	517	53.0
First born (N = 975)	456	46.8
Day care attendance (with ≥ 2 children, N = 975)	699	71.7
Pets (yes)		
Dog (N = 970)	196	20.2
Cat (N = 970)	219	22.6
Smoking during pregnancy (N = 975)	102	10.5
Passive smoking first year (N = 820)	74	7.6
Atopy child (N = 740)	96	13.0
Maternal atopy (N = 727)	297	40.9
Paternal atopy (N = 555)	257	46.3
Maternal allergic disease(s)* (N = 940)	333	35.4
Paternal allergic disease(s)* (N = 935)	201	21.5
Parent-reported eczema in child in first year (N = 932)	227	24.4
Breast feeding duration (N = 976)		
No breast feeding	251	25.7
≤ 6 wk	181	18.5
7–12 wk	160	16.4
13–24 wk	226	23.2
≥ 25 wk	158	16.2
Birth weight (kg, N = 972)		
Mean	3.352	
Lowest	0.830	
Highest	4.980	
Low birth weight (≤ 2.5 kg)	47	4.8
Duration of pregnancy (wk, N = 974)		
Mean	39	
Lowest	25	
Highest	44	
Prematurity (≤ 37 wk)	78	8.0
Use of antibiotics during pregnancy (N = 952)	183	19.2
Use of antibiotics by child first 12 months (N = 926)	594	64.1
Use of antibiotics first 12 months (≥ 2 courses, N = 926)	335	36.2

Atopy was defined as having at least one positive specific IgE.

Descriptive statistics were carried out using all available data for each of the variables.

*Doctor diagnosed asthma and/or eczema and/or hay fever.

Eczema

Parents reported one or more episodes of eczema in 227 (24.4%) of the subjects during the first year of life. At the age of 1 yr, 751 of 976 children (76.9%) visited the study centre for a medical examination. According to the study doctor, 59 (7.9%) of them showed signs of eczema at the time of the visit.

The cumulative incidence of eczema was significantly higher in atopic children [51 of 95 (53.7%)] than in non-atopic children [133 of 631 (21.1%); OR 4.3, 95% CI: 2.8–6.8; $p < 0.01$]. In addition, 27.7% of the children with eczema were atopic (vs. 8.1% in the group without eczema).

In Table 2 determinants of parent-reported eczema in the first year of life are shown. In univariate analyses, children who were ever breast-fed had a slightly but non-significantly increased risk on eczema when compared with children who were never breast-fed (OR 1.3, 95% CI: 0.9–1.8, $p = 0.22$). Duration of BF was

Table 2. Determinants of parent-reported eczema during the first year of life

	Eczema, n (%)	No eczema, n (%)	Crude OR (95% CI)	p-Value
Breast feeding ever/never	177 (78.0)	521 (73.9)	1.3 (0.9–1.8)	0.22
Breast feeding duration (wk)				
Never	50 (22.0)	184 (26.1)	1.0 (ref.)	
1–6	40 (17.6)	133 (18.9)	1.1 (0.7–1.8)	0.67
7–12	38 (16.7)	112 (15.9)	1.2 (0.8–2.0)	0.37
≥13	99 (43.6)	276 (39.1)	1.3 (0.9–1.9)	0.16
Maternal eczema*	49 (22.1)	96 (14.1)	1.7 (1.2–2.5)	0.01
Paternal eczema*	28 (12.7)	38 (5.6)	2.5 (1.5–4.1)	<0.01
Maternal asthma*	17 (7.6)	49 (7.0)	1.1 (0.6–1.9)	0.79
Paternal asthma*	22 (9.8)	35 (5.0)	2.0 (1.2–3.6)	0.01
Maternal hay fever*	57 (25.7)	140 (20.3)	1.4 (1.0–1.9)	0.09
Paternal hay fever*	40 (17.9)	77 (11.2)	1.7 (1.1–2.6)	0.01
Atopy child	51 (27.7)	44 (8.1)	4.3 (2.8–6.8)	<0.01
Atopy father	71 (51.8)	180 (44.3)	1.4 (0.9–2.0)	0.13
Atopy mother	91 (49.5)	200 (37.8)	1.6 (1.1–2.3)	0.01
Prematurity (≥37 wk)	15 (6.6)	59 (8.4)	0.8 (0.4–1.4)	0.39
Birth weight ≤ 2.5 kg	7 (3.1)	36 (5.1)	0.6 (0.3–1.3)	0.21
Educational level mother (high)	164 (81.6)	429 (71.9)	1.7 (1.2–2.6)	0.01
Maternal age (>25 yr)	224 (98.7)	671 (95.2)	3.8 (1.2–12.4)	0.02
Gender (male)	132 (58.1)	359 (50.9)	1.3 (1.0–1.8)	0.06
Older siblings	119 (52.4)	384 (54.5)	0.9 (0.7–1.2)	0.58
Smoking in pregnancy	21 (9.3)	76 (10.8)	0.8 (0.5–1.4)	0.51
Passive smoking in pregnancy	64 (28.2)	259 (36.8)	0.7 (0.5–0.9)	0.02
Passive smoking child first year	21 (10.3)	52 (8.7)	1.2 (0.7–2.1)	0.49
Contact with dogs (yes)	32 (14.2)	151 (21.6)	0.6 (0.4–0.9)	0.02
Contact with cats (yes)	47 (20.8)	162 (23.1)	0.9 (0.6–1.3)	0.46
Day care attendance	170 (74.9)	497 (70.6)	1.2 (0.9–1.7)	0.21
Antibiotics in pregnancy	57 (25.8)	118 (17.2)	1.7 (1.2–2.4)	0.01
Antibiotics first 12 months	87 (39.4)	243 (35.4)	1.2 (0.9–1.6)	0.28

Numbers (%), crude ORs with 95% CI and p-values for eczema group vs. no eczema group.

*Doctor diagnosed.

positively, though not significantly, associated with the occurrence of eczema in the first year [ORs with 95% CIs: 1.1 (0.7–1.8), 1.2 (0.8–2.0) and 1.3 (0.9–1.9) for durations of 1–6 wk, 7–12 wk and more than 13 wk, respectively]. Eczema of the child was significantly (positively) associated with atopy of the child, maternal atopy and eczema, while maternal asthma had no effect on the occurrence of eczema. Paternal asthma, eczema and hay fever significantly increased the risk for development of eczema of the child. Furthermore, important risk factors for eczema were male gender, maternal age (> 25 yr vs. younger), educational level (high vs. low) and use of antibiotics during pregnancy, whereas regular contact with dogs and passive smoking during pregnancy were inversely associated with eczema.

In multiple regression analysis, the association between BF duration and eczema was adjusted for co-variables which were considered to be potential confounders: maternal and paternal atopy, pregnancy duration, maternal educational level and age, active and passive smoking during pregnancy, passive smoking of the child during the first year, gender, postnatal contact with pets,

use of antibiotics during pregnancy and first year, parity and day care attendance (Table 3). After stepwise removal of co-variables from the regression model BF had no statistically significant effect on eczema during the first year of life (adj OR 0.8, 95% CI: 0.4–1.3, $p = 0.32$; adj OR 0.8, 95% CI: 0.5–1.3, $p = 0.36$ and adj OR 1.0, 95% CI: 0.6–1.5, $p = 0.82$ for BF duration of 1–6 wk, 7–12 wk and ≥13 wk, respectively). Independent significant risk factors for eczema during the first year in the final model were maternal atopy (adj OR 1.9, 95% CI: 1.3–2.7, $p < 0.01$) and educational level (adj OR 1.6, 95% CI: 1.1–2.5, $p = 0.03$), use of antibiotics during pregnancy (adj OR 1.8, 95% CI: 1.2–2.7, $p = 0.01$) and passive smoking of the child during the first year (adj OR 1.8, 95% CI: 1.0–3.1, $p = 0.06$). Regular postnatal contact with dogs was inversely associated with eczema (adj OR 0.6, 95% CI: 0.4–0.9, $p = 0.02$).

Parental atopy

After stratification of the study population by atopic status of the parents BF was associated with increased risks for eczema in children of

Table 3. Determinants of parent-reported eczema during the first year of life

	OR	95% CI	p-value
<i>Full model</i>			
Breast feeding duration (wk)			
Never	1.0	(ref.)	
1–6	0.8	0.4–1.4	0.40
7–12	0.7	0.4–1.3	0.29
≥13	1.0	0.6–1.5	0.88
Atopy father	1.4	0.9–2.2	0.09
Atopy mother	1.9	1.3–2.8	<0.01
Prematurity (≤ 37 wk)	0.9	0.4–1.8	0.66
Educational level mother (high)	1.5	0.9–2.4	0.09
Maternal age (>25 yr)	2.0	0.6–7.2	0.29
Gender (male)	1.4	1.0–2.0	0.06
Older siblings	0.8	0.6–1.2	0.35
Smoking in pregnancy	1.2	0.9–1.7	0.18
Passive smoking in pregnancy	0.7	0.4–1.0	0.05
Passive smoking child (first year)	2.0	1.1–3.8	0.03
Contact with dogs (yes)	0.6	0.4–1.0	0.04
Contact with cats (yes)	1.0	0.6–1.5	0.85
Day care attendance	1.3	0.8–1.9	0.27
Antibiotics in pregnancy	1.9	1.3–2.9	<0.01
Antibiotics first 12 months	1.1	0.8–1.5	0.67
<i>Final model</i>			
Breast feeding duration (wk)			
Never	1.0	(ref.)	
1–6	0.8	0.4–1.3	0.32
7–12	0.8	0.5–1.3	0.36
≥13	1.0	0.6–1.5	0.82
Atopy mother	1.9	1.3–2.7	<0.01
Educational level mother (high)	1.6	1.1–2.5	0.03
Antibiotics in pregnancy	1.8	1.2–2.7	0.01
Passive smoking child (first year)	1.8	1.0–3.1	0.06
Contact with dogs (yes)	0.6	0.4–0.9	0.02

Adjusted ORs with 95% CI and p-values for eczema group vs. no eczema group. Final model after backward stepwise regression of full model.

non-atopic parents [adj ORs with 95% CIs: 2.1 (0.4–10.6), $p = 0.35$; 2.2 (0.4–11.3), $p = 0.35$ and 1.9 (0.4–8.5), $p = 0.38$ for BF duration of 1–6 wk, 7–12 wk and ≥ 13 wk, respectively], whereas in children of atopic parents a decreased risk for eczema was found [adj ORs with 95% CIs: 0.6 (0.3–1.3), $p = 0.22$; 0.7 (0.3–1.4), $p = 0.26$ and 0.9 (0.5–1.7), $p = 0.76$]. However, ORs were not statistically significant (Fig. 1). Moreover, the interaction term of BF and parental atopy, assessed in the total study population, appeared to be non-significant ($p = 0.18$).

Discussion

The results of our study in a prospective birth cohort showed that BF has no significant effect on the prevalence of eczema in the first year of life. After stratification of our study population by parental atopy we found an inverse relationship between BF and eczema among children with atopic parents, whereas a positive association existed among children with non-atopic

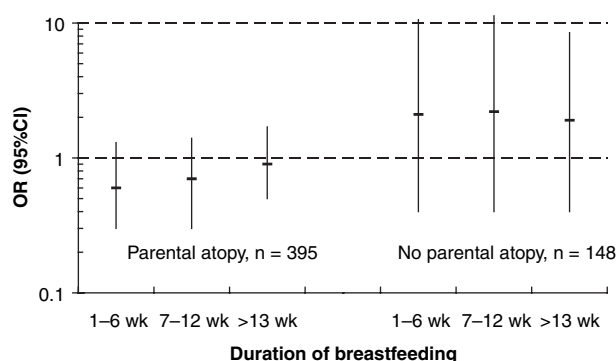


Fig. 1. Associations between duration of breast feeding and parent-reported eczema during the first year of life in subgroups of children with and without parental atopy. Adjusted ORs* with 95% CI (y-axis logarithmic scale). *Odds ratio adjusted for gender, maternal education, active and passive smoking during pregnancy, passive smoking of the child during the first year, pets, pregnancy duration, use of antibiotics during pregnancy and first year, parity and day care attendance.

parents; however, these associations were not statistically significant.

Breast feeding rates

In our study population 74% of the children ever received BF, compared with 92% of the infants in the German Multicenter Allergy Study (MAS-study; 11). At 3 months-of-age 35% of the children in our study were still breast-fed, which is comparable with the study by Kools et al. in the Netherlands (23). Countries with the highest BF rates in the 1990s were Denmark, Sweden and Norway, with rates of 80% at the age of 3 months (8, 24).

At present BF is recommended for prevention of allergic diseases, especially in children with atopic parents (9, 17). Therefore, one might have expected a significant association between allergic disease of the mother and BF, but we did not find this association. However, it appeared that allergic mothers are nursing longer (data not shown), which was also found by Bergmann et al. (11).

Definition of eczema

The terminology used by researchers and doctors to characterize allergic diseases in general, and allergic skin disorders in particular, is confusing. We used the term 'eczema' in accordance with the Report of the Nomenclature Review Committee of the World Allergy Organization (October 2003), stating the disease to be referred to as 'eczema' as long as the immunological mechanism of eczema is unclear. This term has been

proposed to replace the provisional terms 'atopic eczema' and 'atopic dermatitis', which are often inaccurately used in medical literature (25).

Breast feeding and eczema

The relationship between BF and allergic diseases still seems to be unclear. Several studies have found a protective effect of BF against the development of allergies (5–9). A randomized intervention study on the promotion of BF in Belarus by Kramer et al. (5) demonstrated a significant reduction of the risk of atopic eczema during the first year in children from intervention sites (where mothers were assisted in initiating and maintaining lactation and BF, resulting in significantly higher rates, duration and exclusivity of BF) compared with control sites: 3.3% vs. 6.6%. However, the atopic status of the children was not confirmed by objective measurements, such as IgE analysis. Kull et al. also showed a protective effect of BF on the development of allergic diseases during the first 2 yr (8). Reduction of this risk was more prominent in the group with exclusive BF, although partial BF appeared to be protective as well. Furthermore, they indicated that BF postpones the onset of symptoms possibly related to allergic disease, but we could not confirm this finding for eczema in our study population (data not shown).

In contrast, few studies have been published in which BF is associated with an increased risk for the development of allergic diseases, particularly atopic eczema (10–13). Bergmann et al. reported that each additional month of BF elevated the risk of developing atopic eczema in the first 7 yr by 3%, even after adjustment for potential confounders (11). However, they could not exclude reverse causation, meaning that mothers with children who develop eczema tend to breastfeed their children for a longer period of time. In that study the development of eczema was related to any, but not necessarily exclusive BF: half of the children received cow's milk formula in addition to breast milk in the first days of life. According to Böttcher and Jenmalm, the age of introducing formula feeding rather than the duration of BF may be important (26). However, we did not find a relationship between the age of introduction of formula feeding and eczema in our study population (data not shown).

Purvis et al. showed that atopic eczema is positively associated with the duration of BF (13). Furthermore, they found a strong association between eczema at the age of 3.5 yr and parental atopy (paternal as well as maternal atopy). We found a significant association only with maternal

atopy, which is in accordance with findings from other studies (27, 28), including a previous publication based on the PIPO-project by Hagendorens et al. (29). According to Kurzius-Spencer et al. (28), this may be explained by certain exposures *in utero*, as maternal colds, active eczema and high maternal IgE during pregnancy.

Parental atopy

After stratification of our study population by parental atopy, it appeared that BF was inversely associated with the occurrence of eczema in the subgroup with atopic parents, whereas in the subgroup with non-atopic parents positive associations were found. Although these associations were not statistically significant, they suggest that the effect of BF on allergy may depend on the atopic status of the parents as this has been found in previous studies (14–17). A meta-analysis of 18 prospective studies on BF and atopic dermatitis in childhood by Gdalevich et al. in 2001 yielded support for a protective effect of exclusive BF during the first 3 months in the prevention of atopic dermatitis in children with a positive family history of atopy (17). This protection was non-existent in children without atopic heredity. Two additional studies published after this review demonstrated incongruent effects of BF on atopic disease: in children with atopic heredity it protected against atopic dermatitis (14) and atopy (15), while in children without atopic heredity BF increased the risk of these diseases. In contrast, Wright et al. reported in 1999 that BF was associated with lower total serum IgE at age 6 and 11 yr only among children whose mothers were in the two lower tertiles of IgE, whereas in children whose mothers were in the highest tertile of IgE, BF was associated with higher IgE levels (16).

Maternal breast milk composition

The different effects of BF among infants with and without maternal atopy may in part be explained by differences in the FA composition of breast milk of atopic and non-atopic mothers. According to Yu et al., breast milk FA composition is disturbed in atopic mothers (30). Several studies have analysed the association between breast milk FA composition and allergic diseases in childhood. Some of them reported that the disturbed composition of FA in maternal milk is related to the atopic development in the children (18–20), whereas Oddy et al. found that milk FAs in high-risk children were a significant modulator for non-atopic

eczema, but not for atopic eczema or atopy among infants at 6 months-of-age (21). A similar relationship of breast milk FA with the development of allergic symptoms, but not with atopic sensitization, is reported by Wijga et al., suggesting different mechanisms of FA intake to sensitization and allergic symptoms (22). Unfortunately, we did not collect breast milk samples to assess the FAs composition in relation to development of eczema in our study population.

Advantages and limitations of the study

The strength of our study is the collection of prenatal and postnatal exposure data, thus before and during the onset of disease. Moreover, the design of the data collection process allowed us to include infants both with and without parental allergy. In addition, IgE measurements from the parents enabled us to identify parental atopy more reliably than by questionnaire data only.

On the other hand, some limitations may have affected our results. First, we have used partial (not exclusive) BF, which could have weakened our associations. Secondly, the outcome measure used was 'parent-reported' eczema, which was not confirmed by a doctor. For this reason, prevalence of eczema may be higher than in some studies. Harris et al. clearly demonstrated that the prevalence of eczema depends on its definition, varying from 14% by strict UK diagnostic criteria to 45% if reported by the mother (27). However, the higher prevalence of the eczema in our study population is most likely independent from BF status; therefore, misclassification is non-differential, leading to an underestimation of true associations.

Another reason for the high prevalence of eczema in our study may be a selective withdrawal from the study by non-allergic parents, as has been demonstrated previously. As a result, the proportion of atopic children in our study may be higher than would be expected from the general population. This means that the study population does not closely represent the Belgian population. However, there is no reason to believe that this selective participation affects the associations studied.

Finally, misclassification may also have occurred in defining children (or parents) as non-atopic because of the limited number of inhalant and food allergens tested (which is common in most epidemiological studies). This will, however, also be unrelated to the BF status.

In conclusion, we did not find a significant association between BF and eczema during the

first year of life. However, our results show that the effects of BF on eczema are different among children with atopic vs. non-atopic parents.

Acknowledgments

We thank the study families for their participation, and all PIPO-study personnel and nurses for the recruitment and follow-up of the families: Prof. P. Vermeire, Prof. H. Van Bever, V. Nelen, E. Vandervaeren, L. Thijs, M. Duym, G. Meysen, R. Vroom, D. Stappers, K. Vandekerckhove, R. Heyndrickx, F. Willekens, C. Daenen, P. Beyltjens, H. Nafez.

This study was supported by grants from the Fund for Scientific Research Flanders, Belgium (no. 7.0015.00) and the Flemish Government (PBO98/26/143). Pharmacia Diagnostics, Belgium kindly provided the Immuno-CAP.

References

1. GOLDMAN AS. The immune system of human milk: antimicrobial, antiinflammatory and immunomodulating properties. *Pediatr Infect Dis J* 1993; 12: 664–71.
2. GILLMAN MW, RIFAS-SHIMAN SL, CAMARGO CA JR, et al. Risk of overweight among adolescents who were breastfed as infants. *JAMA* 2001; 285: 2461–7.
3. SINGHAL A, COLE TJ, FEWTRILL M, LUCAS A. Breast-milk feeding and lipoprotein profile in adolescents born preterm: follow-up of a prospective randomised study. *Lancet* 2004; 363: 1571–8.
4. GRULÉE CG, SANFORD HN. The influence of breast and artificial feeding on infantile eczema. *J Pediatr* 1936; 32: 223–5.
5. KRAMER MS, CHALMERS B, HODNETT ED, et al. Promotion of Breastfeeding Intervention Trial (PROBIT): a randomized trial in the Republic of Belarus. *JAMA* 2001; 285: 413–20.
6. SAARINEN UM, KAJOSAARI M. Breastfeeding as prophylaxis against atopic disease: prospective follow-up study until 17 years old. *Lancet* 1995; 346: 1065–9.
7. VAN ODIJK J, KULL I, BORRES MP, et al. Breastfeeding and allergic disease: a multidisciplinary review of the literature (1966–2001) on the mode of early feeding in infancy and its impact on later atopic manifestations. *Allergy* 2003; 58: 833–43.
8. KULL I, WICKMAN M, LILJA G, NORDVALL SL, PERSHAGEN G. Breast feeding and allergic diseases in infants—a prospective birth cohort study. *Arch Dis Child* 2002; 87: 478–81.
9. MURARO A, DREBORG S, HALKEN S, et al. Dietary prevention of allergic diseases in infants and small children: Part III. Critical review of published peer-reviewed observational and interventional studies and final recommendations. *Pediatr Allergy Immunol* 2004; 15: 291–307.
10. SEARS MR, GREENE JM, WILLAN AR, et al. Long-term relation between breastfeeding and development of atopy and asthma in children and young adults: a longitudinal study. *Lancet* 2002; 360: 901–7.
11. BERGMANN RL, DIEPGEN TL, KUSS O, et al. Breastfeeding duration is a risk factor for atopic eczema. *Clin Exp Allergy* 2002; 32: 205–9.
12. MIYAKE Y, YURA A, IKI M. Breastfeeding and the prevalence of symptoms of allergic disorders in Japanese adolescents. *Clin Exp Allergy* 2003; 33: 312–6.

13. PURVIS DJ, THOMPSON JM, CLARK PM, et al. Risk factors for atopic dermatitis in New Zealand children at 3.5 years of age. *Br J Dermatol* 2005; 152: 742–9.
14. BENN CS, WOHLFAHRT J, AABY P, et al. Breastfeeding and risk of atopic dermatitis, by parental history of allergy, during the first 18 months of life. *Am J Epidemiol* 2004; 160: 217–23.
15. SILTANEN M, KAJOSAARI M, POUSSA T, SAARINEN KM, SAVILAHTI E. A dual long-term effect of breastfeeding on atopy in relation to heredity in children at 4 years of age. *Allergy* 2003; 58: 524–30.
16. WRIGHT AL, SHERRILL D, HOLBERG CJ, HALONEN M, MARTINEZ FD. Breast-feeding, maternal IgE, and total serum IgE in childhood. *J Allergy Clin Immunol* 1999; 104: 589–94.
17. GDALEVICH M, MIMOUNI D, DAVID M, MIMOUNI M. Breast-feeding and the onset of atopic dermatitis in childhood: a systematic review and meta-analysis of prospective studies. *J Am Acad Dermatol* 2001; 45: 520–7.
18. WRIGHT S, BOLTON C. Breast milk fatty acids in mothers of children with atopic eczema. *Br J Nutr* 1989; 62: 693–7.
19. DUCHEN K, CASAS R, FAGERAS-BOTTCHER M, YU G, BJORKSTEN B. Human milk polyunsaturated long-chain fatty acids and secretory immunoglobulin A antibodies and early childhood allergy. *Pediatr Allergy Immunol* 2000; 11: 29–39.
20. DUCHEN K, BJORKSTEN B. Polyunsaturated n-3 fatty acids and the development of atopic disease. *Lipids* 2001; 36: 1033–42.
21. ODDY WH, PAL S, KUSEL MM, et al. Atopy, eczema and breast milk fatty acids in a high-risk cohort of children followed from birth to 5 yr. *Pediatr Allergy Immunol* 2006; 17: 4–10.
22. WIJGA AH, van HOUWELINGEN AC, KERKHOF M, et al. Breast milk fatty acids and allergic disease in preschool children: the Prevention and Incidence of Asthma and Mite Allergy birth cohort study. *J Allergy Clin Immunol* 2006; 117: 440–7.
23. KOOLS EJ, THIJIS C, KESTER AD, van den BRANDT PA, de VRIES H. A breast-feeding promotion and support program a randomized trial in The Netherlands. *Prev Med* 2005; 40: 60–70.
24. HUNTER HH. Why many more women breastfeed in Norway than in Britain. New generation. *J NCT* 1996; 15: 26–7.
25. JOHANSSON SG, BIEBER T, DAHL R, et al. Revised nomenclature for allergy for global use: report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. *J Allergy Clin Immunol* 2004; 113: 832–6.
26. BOTTCHER MF, JENMALM MC. Breastfeeding and the development of atopic disease during childhood. *Clin Exp Allergy* 2002; 32: 159–61.
27. HARRIS JM, CULLINAN P, WILLIAMS HC, et al. Environmental associations with eczema in early life. *Br J Dermatol* 2001; 144: 795–802.
28. KURZIUS-SPENCER M, HALONEN M, LOHMAN IC, MARTINEZ FD, WRIGHT AL. Prenatal factors associated with the development of eczema in the first year of life. *Pediatr Allergy Immunol* 2005; 16: 19–26.
29. HAGENDORENS MM, BRIDTS CH, LAUWERS K, et al. Perinatal risk factors for sensitization, atopic dermatitis and wheezing during the first year of life (PIPO study). *Clin Exp Allergy* 2005; 35: 733–40.
30. YU G, DUCHEN K, BJORKSTEN B. Fatty acid composition in colostrum and mature milk from non-atopic and atopic mothers during the first 6 months of lactation. *Acta Paediatr* 1998; 87: 729–36.