

CORRESPONDENCE

Breast feeding and early life immunomodulation

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To the Editor,

We have read with interest the article from Belderbos et al. (1) suggesting the ability of breastfeeding to down-modulate the secretion of TNF- α and IL-10 by white blood cells in term children during the first month of life. Also very recently, we have reported the existence of an inverse association between duration of breastfeeding and levels of IL-10 and RANTES secreted by the upper respiratory tract 1 year after birth in preterm children (2). A total of 77 children were recruited in our study. Gestational age (weeks) was (mean, SD) 31.9 (2.9). Sex composition was (women/men): 35/38. Weight at birth (kg) was 1.8 (0.5). Length at birth (cm) was 42.5 (4.2). Eight children had broncho-pulmonary dysplasia at birth. The most frequent accompanying condition was the presence of personal ($n = 16$) or familial antecedents ($n = 32$) of atopic dermatitis. The majority of the children received breastfeeding (60%) for an average of 5.4 months after birth. Cytokines were measured using the 27-plex Bio-Rad assay (Hercules, CA, USA) on a Luminex platform (Austin, TX, USA), including IL-1 receptor antagonist (IL-1RA), IL-9, IL-15, Eotaxin, human fibroblast growth factor-basic (FGF-b): IFN-inducible protein 10 (IP-10), macrophage inflammatory protein 1a (MIP-1 α), platelet-derived growth factor (PDGF-BB), regulated upon activation, normal T cell expressed, and secreted protein (RANTES), vascular endothelial growth factor (VEGF), IL1 β , IL-6, IL-8, IL-7, IL-17, granulocyte colony-stimulating factor (G-CSF), monocyte chemoattractant protein 1 (MCP-1), macrophage inflammatory protein 1b (MIP-1 β), IL-2, IL-4, IL-5, IL-10, IL-12, IL-13, granulocyte macrophage colony-stimulating factor (GM-CSF), IFN- γ and tumor necrosis factor alpha (TNF- α). Interestingly, duration of breastfeeding (in months) inversely correlated with levels in nasopharyngeal aspirates of IL-1 β (Spearman correlation coefficient, p): (-0.254, 0.035), G-CSF (-0.236, 0.050), MIP-1 β (-0.250, 0.039), IL-10 (-0.323, 0.007), and TNF- α (-0.254, 0.035) (Fig. 1), and also with RANTES, IL-6, IL-17 at the level ($p < 0.1$). Belderbos et al. normalized cytokines by means of logarithmic transformation. Reproducing this approach, we now used logarithmic values for cytokines. Univariate linear regression analysis was performed again to evaluate the relationship between breastfeeding and cytokine levels 1 year after birth. Potential confounding variables were also evaluated in the univariate analysis: gestational age, sex, weight at birth, height at birth, [breastfeeding (duration in months)], bronchopulmonary dysplasia, atopic dermatitis, smoking habit at home, assistance to daycare, siblings at daycare or at school, number of people living at home, sibillances needing of treatment in the first year of life, [prophylaxis with PVZ (three or more doses)], symptoms of respiratory

infection in the first year of life observed by the pediatrician, and necessity of hospitalization in the first year of life. Those variables yielding p values < 0.2 in the univariate analysis were entered into a further multivariate analysis. After adjusting for potential confounding variables, duration of breastfeeding was inversely associated with levels of RANTES and IL-10 (Table 1). In turn, the variable (siblings at daycare or at school) was directly associated with IL-10 levels and the variable (prophylaxis with PVZ) was inversely associated with levels of this cytokine. Both RANTES and IL-10 are involved in allergy/asthma pathogenesis.

In conclusion, these works are pioneer in providing biological evidence on the immuno-modulatory ability of breastfeeding in early life. This activity could be explained by the protective effect of breastfeeding against infections (3, 4). Alternatively, breastfeeding-induced protection might rely on tolerance induction to common environmental and dietary antigens because of antigen transfer across mammary epithelium or to the presence of factors in breast milk influencing neonatal immune system maturation, including immunoglobulins, oligosaccharides, and antimicrobial proteins/peptides (5). These results could explain thus the potential protective effect of breastfeeding against asthma/allergy.

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Table 1 Multivariate analysis: association between duration of breastfeeding in months and cytokine levels in nasopharyngeal aspirates 1 year after birth

RANTES				IL-10			
	<i>B</i>	SE	p		<i>B</i>	SE	p
Atopic dermatitis	−0.43	0.25	n.s.	Gestational age	0.00	0.03	n.s.
Assistance to daycare	−0.28	0.27	n.s.	Assistance to daycare	0.22	0.18	n.s.
Siblings at daycare or at school	0.45	0.26	n.s.	Siblings at daycare or at school	0.32	0.15	0.040
Number of people living at home	0.16	0.10	n.s.	Prophylaxis with PVZ	−0.30	0.15	0.050
Sibilances needing of treatment in the first year of life	0.12	0.20	n.s.	Necessity of hospitalization in the first year of life	−0.26	0.14	n.s.
Breastfeeding (duration in months)	−0.08	0.03	0.005	Breastfeeding (duration in months)	−0.04	0.02	0.017

B, coefficient of regression; SE, standard error of *B*.

All the variables yielded $p < 0.2$ in the univariate analysis.

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