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Cow's Milk Allergic Infants on Elemental Formula Maintain Adequate Mineral Status Despite Using Acid-suppressive Drugs

To the Editor: We recently presented data in this Journal showing that cow's milk allergic infants who received an amino acid–based formula (AAF) for 16 weeks as oral feeding had adequate mineral status (1). One factor that may negatively affect mineral solubility and bioavailability and hence mineral status, is a high gastric pH (2). Therefore, we currently present data on mineral status of a subgroup of infants on AAF receiving acid-suppressive drugs.

We analysed retrospectively the data of infants (0–8 months) with confirmed immunoglobulin E or non-immunoglobulin E–mediated cow's milk allergy who were randomized between 2008 and 2012 in a double-blind fashion to either an AAF with or without synbiotics (3). In- and exclusion criteria of the study and baseline characteristics of the enrolled infants have been reported before in our original paper (1). Details about the composition of the study formulae (Neocate; SHS International Ltd, Nutricia Advanced Medical Nutrition, Liverpool, UK) can be found in Table 1.

Serum concentrations of phosphorus, calcium, and magnesium were determined at baseline (n = 82) and after 16 weeks (n = 66) on AAF and compared to age-specific reference ranges. Subgroup analysis was performed for infants who were receiving acid-suppressive drugs (proton-pump-inhibitors/H_2-antagonists), that is, approximately one-third (35%) of our sample. Between-group comparisons were made by 2-tailed Student *t* tests. *P* values >0.05 were considered as not significant.

Serum concentrations of phosphorus, calcium, and magnesium for the total population and for the subgroups of infants receiving or not receiving acid-suppressive drugs are presented in Tables 2 and 3. After 16 weeks, mineral concentrations of all infants were within the reference range.

TABLE 1. Macronutrient and mineral profile of study products per 100 kcal of prepared product

	Neocate with synbiotics	Neocate without synbiotics*
Energy	67 kcal/100 mL	67 kcal/100 mL
Macronutrients		
Proteins, g	2.8	3.1
Carbohydrates, g	11.3	11.7
Fats, g	4.8	4.5
Dietary fibre, g	1.1	–
Bifidobacterium breve M16-V, CFU	2.11×10^9	–
Minerals		
Sodium, mg	40	37
Potassium, mg	105	155
Chloride, mg	75	77
Calcium, mg	90	124
Phosphorus, mg	63	93
Magnesium, mg	11.2	12.4
Iron, mg	1.5	1.9
Zinc, mg	1.1	1.7
Copper, μg	76	124
Manganese, μg	76	90
Selenium, μg	2.8	3.7
Iodine, μg	17.5	15.4
Mineral sources	Calcium phosphate dibasic, tripotassium citrate, sodium chloride, magnesium chloride, tricalcium citrate, magnesium L-aspartate, ferrous slphate, zinc sulphate, calcium D-pantothenate, manganese sulphate, cupric sulphate, potassium iodide, chromium chloride, sodium selenite, sodium molybdate	

* Differences in blood chemistry parameters (at baseline, week 16, and change from baseline) between the study products have been analysed before and were not found to be statistically significant or clinically relevant (1,3) and are therefore presented for the combined (Neocate with or without synbiotics) group.

Our data show that, although doses, compliance, and the neutralizing effect of the acid-suppressive drugs were not measured and infants were not randomized for acid-suppressive drug use, cow's milk allergic infants orally fed with AAF for 16 weeks maintain target serum concentrations of phosphorus, calcium, and magnesium even when receiving acid-suppressive drugs. Regular review of the ongoing need for acid-suppressive drugs remains recommended.

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TABLE 2. Serum concentrations (mean, 95% confidence interval) of phosphorus (P), calcium (Ca), and magnesium (Mg) and number (n, %) of infants having P, Ca, and Mg concentration below the lowest range of the reference value at baseline

				Acid-suppressive drugs						
	Total population (n = 82)			Users (n = 29)			Non-users (n = 53)			
	Mean	95% CI	n (%)	Mean	95% CI	n (%)	Mean	95% CI	n (%)	*P* value: users vs nonusers
P, mmol/L	2.05	2.00–2.11	1 (1%)	2.10	2.00–2.19	0	2.03	1.96–2.10	1 (2%)	ns
Ca, mmol/L	2.67	2.64–2.70	1 (1%)	2.67	2.63–2.71	0	2.66	2.62–2.71	1 (2%)	ns
Mg, mmol/L	0.95	0.93–0.96	0	0.95	0.93–0.97	0	0.94	0.93–0.96	0	ns

Reference ranges—*P*: 1.36–2.62 (<1 years) and 1.03–1.97 (≥1 years) mmol/L; Ca: 2.25–2.74 mmol/L; Mg: 0.70–0.98 (<30 days), 0.66–1.03 (males, ≥30 days), and 0.78–0.98 (females, ≥30 days) mmol/L.
ns = not significant.

TABLE 3. Serum concentrations (mean, 95% confidence interval) of phosphorus (P), calcium (Ca), and magnesium (Mg) and number (n, %) of infants having P, Ca, and Mg concentration below the lowest range of the reference value after 16 weeks intervention with an amino acid–based formula

				Acid-suppressive drugs						
	Total population (n = 66)			Users (n = 25)			Non-users (n = 41)			
	Mean	95% CI	n (%)	Mean	95% CI	n (%)	Mean	95% CI	n (%)	*P* value: users vs nonusers
P, mmol/L	1.96	1.91–2.01	0	1.95	1.88–2.03	0	1.97	1.90–2.04	0	ns
Ca, mmol/L	2.62	2.59–2.65	0	2.63	2.59–2.68	0	2.61	2.58–2.65	0	ns
Mg, mmol/L	0.95	0.94–0.97	0	0.96	0.94–0.99	0	0.95	0.92–0.97	0	ns

Reference ranges—*P*: 1.36–2.62 (<1 years) and 1.03–1.97 (≥1 years) mmol/L; Ca: 2.25–2.74 mmol/L; Mg: 0.70–0.98 (<30 days), 0.66–1.03 (males, ≥30 days), and 0.78–0.98 (females, ≥30 days) mmol/L.
ns = not significant.

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HLA-DQB1*02 Allele in First-degree Relatives of Patients With Celiac Disease

To the Editor: The recent article published by Lopes et al (1) investigated the frequency of celiac disease (CD) in the first-degree relatives (FDR) of affected patients and their HLA genetic predisposition. There are 2 specific findings from this study, that captured my attention, in light of the results of previous studies published by our group.

First, the authors found that the odds ratio (OR) for CD in their FDR cohort was equal to 5.1 for HLA-DQB1*02 homozygous patients, compared to otherwise genetically predisposed FDR. Through a meta-analysis, we reported a risk gradient to develop CD according to the HLA genetic background, whereby the highest risk was displayed by the carriers of a double copy of the HLA-DQB1*02 allele (OR = 5.3–5.4 compared to the general pediatric population). Actually, we found that a single copy of HLA-DQB1*02 had an OR that is not much lower (OR = 3.9–4.6, depending on the remaining HLA-DQ profile) (2). In the present study, it would be an interesting completion to compare the OR between these specific populations of FDR.

Second, all 7 FDR patients with CD seem to be carriers of at least 1 copy of the HLA-DQB1*02 allele, but this is not completely clear from the text, where the authors refer to ''nonhomozygous'' individuals. Indeed, our group suggested that, among genetically susceptible children, almost all children with CD are carriers of at least 1 copy of the HLA-DQB1*02 allele (>95%, probably) (2,3). This knowledge may have some practical impact for CD screening strategies, if further supported by additional, larger and independent studies.

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