

Serum carotenoids and atopy among children of different ethnic origin living in Germany

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The manifestation of atopy in early life is thought to be influenced by the diet. We hypothesized that the previously reported lower prevalence of atopy among Turkish immigrant children in Germany might be related to a different pattern of serum carotenoids. Serum carotenoid concentrations were measured in pre-school children of different ethnic origin from Berlin, D. German children (D, N = 49) were compared to Turkish children with well (TR-D, N = 32) or weak cultural adaptation (TR-TR, N = 41). Serum levels of pro-vitamin A carotenoids (α - and β -carotene, β -cryptoxanthin) and non-pro-vitamin A carotenoids (lutein, zeaxanthin, lycopene) were measured by high performance liquid chromatography. Serum IgE to common inhalant allergens was measured by immunoassay. Median levels of pro-vitamin A carotenoids were lower in Turkish children if compared to German children: D 135 μ g/L, TR-D 100 μ g/L ($p = 0.025$), TR-TR 82 μ g/L ($p = 0.001$). By contrast, median levels of non-pro-vitamin A carotenoids were not higher in German children. The ratio of pro-vitamin A to non-pro-vitamin A carotenoid median levels was highest among D (2.05), lower among TR-D (1.32; $p = 0.001$) and lowest among TR-TR (1.26; $p < 0.001$). A higher ratio was not significantly associated with atopy (atopic 1.79, non-atopic 1.36; $p = 0.067$). Pro-vitamin A carotenoids are higher in children originating from a cultural population with a higher prevalence of atopy, but atopy seems not to be directly related to the current carotenoid serum levels in children at school age. The distinct pattern of carotenoid levels among Turkish migrant and German children indicates changed nutrition patterns with acculturation.

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Atopy mainly manifests during the first years of life, and the emergence of allergic sensitisation and disease is thought to be influenced by the diet. The prevalence of atopic disease tends to be less frequent in countries with a less Westernized lifestyle. In migrants moving from these countries to more Westernized countries and adapting to their lifestyle, the prevalence of atopic disease increases (1). Factors like social class, family size, infections and pet ownership do not fully explain these differences (2). Diet changed considerably during the recent decades

in Western countries and coincided with the increase of atopy prevalence. Dietary changes as a result of cultural adaptation among migrants have not been investigated in this respect.

Vitamin A and carotenoids are modulators of allergic sensitisation. A diet rich in vitamin A promotes allergic sensitisation in rodent studies (3, 4). Carotenoid concentrations differ considerably between populations depending on their nationality, gender, nutritional behavior, ethnic background (5) and mainly on individual nutri-

tion (6). Serum level of β -carotene tends to be higher in affluent populations (7).

Supplemental vitamin A and pro-vitamin A carotenoids can be metabolised *in vitro* and *in vivo* into bioactive retinoic acids (8), which activate the nuclear hormone receptors: retinoic acid receptors (RARs) and retinoid X receptors (RXRs). Activation of RAR and RXR pathways lead to enhanced Th2-type cytokine secretion and increased formation of IgE in mice (4). Novel studies by our laboratories described increased concentrations of all-*trans*-retinoic acid after nutritional relevant 2-weeks carrot juice supplementation (high in β -carotene) (8).

Children of Turkish migrants in Germany have a much lower prevalence of atopy than their German peers (9), but they approach the prevalence rate of the latter as cultural adaptation progresses (2). We hypothesized that the pattern of serum carotenoids could differ between children with different cultural background and that these patterns may be related to atopy. In our study, we analyzed carotenoid concentrations in sera of atopic and non-atopic children of German and Turkish origin living in a very similar macroenvironment.

Methods

Study population

The catchment area for this cross-sectional study was Wedding, an inner city district of Berlin, Germany, with 29.7% Turkish immigrants in 1998. Children were recruited prior to school entry for a population-based survey of atopic disease (2). For this study, we included sera from children who were born in Germany and whose parents either were of German or of Turkish nationality. Adaptation of Turkish families to the German culture was assessed by use of the German language at their home (2). Informed written content was obtained from parents, and the study protocol was approved by the institutional ethics committee.

We included all available sera from children with allergic sensitisation to inhalant allergens from three groups: (1) German children; (2) Turkish children with low acculturation; and (3) Turkish children with better cultural adaptation. From each of the groups, we included at random a matching number of sera from the remaining children without allergic sensitisation.

IgE, retinol and carotenoid determination

Serum samples were stored at -20°C until analysis. All sera were screened with a fluores-

cence immunoassay (CAP FEIA; Phadia, Freiburg, Germany) for the presence of specific IgE to common indoor and outdoor inhalant allergens (Phadiatop; Phadia). In the case of a positive test result (IgE titer ≥ 0.35 kU/l), the child was considered to be atopic, and the serum was analyzed for specific IgE to the particular allergens to differentiate sensitisation. Carotenoid and retinol analysis was performed according to a validated procedure (10). Serum levels below the detection limit (1 ng/l) were converted for statistical analysis into 50% of the detection limit. For further evaluation, the levels of the carotenoids α -carotene, β -carotene and β -cryptoxanthin were summarized as pro-vitamin A carotenoids, and the carotenoids lutein, zeaxanthin and lycopene were summarized as non-pro-vitamin A carotenoids.

Statistical analysis

Statistical analysis was performed with SPSS (version 14.0 for PC, SPSS Inc., Chicago, IL, USA). For bivariate analysis, Pearson's chi-squared tests were applied for the association of binary data: Fisher's exact was used when the expected frequency of any cell was less than five. The non-parametric Mann-Whitney *U* test was employed for association of continuous variables. Statistical significance was defined by two-sided alpha level of 0.05.

Results

Study subjects

Sera of 49 German children, 32 well adapted and 17 weakly adapted Turkish children were included in this study. There was no statistically significant group difference in regard to gender or age (data not shown). Forty-one out of 122 children (34%) were atopic, 24 from the German group, 7 from the well adapted and 10 from the weakly adapted Turkish groups.

Serum levels in relation to ethnicity

The median retinol serum levels of the German group and the Turkish groups were similar (Table 1). Pro-vitamin A carotenoid serum levels were significantly lower among well adapted Turkish children ($p = 0.025$) and lowest among weakly adapted Turkish children ($p = 0.001$) than among German children (Table 1). Detailed analysis of pro-vitamin A carotenoids revealed that serum levels of α -carotene, β -carotene and β -cryptoxanthin followed the same trend with

Table 1. Serum levels (median, 5th and 95th percentile) of retinol and carotenoids in relation to acculturation.

	German N = 49	Turkish, well adapted N = 32	Turkish, weakly adapted N = 41
Retinol [mg/L]	0.284 (0.176; 0.421)	0.257 (0.136; 0.508)	0.269 (0.123; 0.397)
Pro-vitamin A carotenoids	0.135 (0.054; 0.540)	0.100 (0.035; 0.292)*	0.082 (0.038; 0.231)**
α-Carotene [mg/L]	0.014 (0.005; 0.066)	0.008 (0.002; 0.041)**	0.006 (0.002; 0.024)***
β-Carotene [mg/L]	0.067 (0.026; 0.326)	0.050 (0.018; 0.195)*	0.038 (0.014; 0.118)***
β-Cryptoxanthin [mg/L]	0.050 (0.011; 0.195)	0.034 (0.011; 0.107)	0.031 (0.009; 0.115)
Non pro-vitamin A carotenoids	0.064 (0.034; 0.115)	0.076 (0.027; 0.196)	0.069 (0.025; 0.169)
Lutein [mg/L]	0.049 (0.028; 0.086)	0.056 (0.022; 0.147)	0.051 (0.019; 0.136)
Zeaxanthin [mg/L]	0.004 (0.002; 0.013)	0.006 (0.002; 0.014)	0.006 (0.002; 0.013)*
Lycopene [mg/L]	0.009 (0.002; 0.032)	0.009 (0.002; 0.042)	0.010 (0.009; 0.028)
Ratio of pro-vitamin A/non pro-vitamin A carotenoids	2.05 (1.37; 3.35)	1.22 (0.98; 1.94)***	1.19 (0.95; 1.54)***

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$ (reference, German children).

Table 2. Serum levels (median, 5th and 95th percentile) of retinol and carotenoids in relation to atopy.

	Nonatopic N = 81	Atopic N = 41
Retinol [mg/L]	0.271 (0.143; 0.432)	0.259 (0.157; 0.393)
Pro-vitamin A [mg/L]	0.105 (0.039; 0.402)	0.116 (0.038; 0.293)
α-Carotene [mg/L]	0.009 (0.002; 0.052)	0.011 (0.003; 0.050)
β-Carotene [mg/L]	0.054 (0.018; 0.223)	0.060 (0.020; 0.141)
β-Cryptoxanthin [mg/L]	0.036 (0.013; 0.144)	0.039 (0.006; 0.094)
Non pro-vitamin A [mg/L]	0.070 (0.033; 0.169)	0.063 (0.023; 0.113)*
Lutein [mg/L]	0.052 (0.025; 0.134)	0.047 (0.020; 0.092)
Zeaxanthin [mg/L]	0.006 (0.002; 0.014)	0.005 (0.002; 0.011)
Lycopene [mg/L]	0.010 (0.002; 0.034)	0.008 (0.002; 0.020)*
Ratio of pro-vitamin A/non pro-vitamin A	1.34 (0.64; 5.35)	1.71 (0.86; 4.13)

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$ (reference, nonatopic children).

lower values among the Turkish children (Table 1). By contrast, non-pro-vitamin A carotenoid serum levels were not higher in German than in Turkish children. Accordingly, detailed analysis of non-pro-vitamin A carotenoids showed slightly lower concentrations in German children in comparison with Turkish children. The ratio of pro-vitamin A to non-pro-vitamin A carotenoid median levels was highest among German children, significantly lower among well adapted Turkish and lowest among weakly adapted Turkish children (Table 1).

Serum levels in relation to atopy

The retinol median serum levels were not significantly different between the atopic and the non-atopic group (Table 2). Likewise, levels of pro-vitamin A carotenoids, taken together or individually, did not significantly differ between atopics and non-atopics, but there was a tendency toward higher concentrations in the atopics (Table 2). Non-pro-vitamin A levels were significantly higher in non-atopics if compared to atopics ($p = 0.035$). The serum level of lycopene

was significantly lower among atopics ($p = 0.021$). The ratio of pro-vitamin A to non-pro-vitamin A serum levels was non-significantly associated with allergic sensitisation ($p = 0.067$).

Discussion

The key finding of this study is a positive association of the pro-vitamin A/non-pro-vitamin A carotenoid ratio in the serum and adaptation to Western culture. As carotenoid serum levels are dependent on individual intake, lower levels of pro-vitamin A carotenoids in well and weakly adapted Turkish children indicate a distinct nutrition pattern, which is altered with adaptation to Western lifestyle. Nutrition of Western culture is usually associated with a diet rich in fat and carbohydrates, and various other studies pointed out that carotenoid pattern and vitamin A levels are drastically changed during Westernization (11).

In this study, retinol serum levels were comparable to levels found in healthy children previously (12), and there was no clear association of retinol and carotenoids with atopy. A non-significant tendency for lower ratios of pro-vitamin A/non-pro-vitamin A carotenoids (atopic 1.79, non-atopic 1.36; $p = 0.067$) was observed. Statistically significant are the lower concentrations of lycopene and the sum of non-pro-vitamin A carotenoids in atopic children, indicating that especially lycopene might protect from atopy, which is in accordance with studies in humans and animals showing an inverse association of serum lycopene and asthma (13, 14). In our study, no coherent association between retinol and individual carotenoids was observed but various tendencies are observable.

We found different carotenoid patterns in children depending on their nationality and their cultural adaptation. These differences in carot-

enoid pattern indicate an alteration during adaptation to Western lifestyle. In addition, carotenoid patterns are altered in chronic inflammation diseases such as atopy (6, 15), because of the fact that carotenoids also act as antioxidants and are destroyed during radical elimination processes. Unfortunately, the carotenoid levels measured in our study just reflect the current levels of these differences.

Investigation of further nutritional biomarkers and up-stream regulators of IgE (defined here as atopy) including IL-4 and IL-13, which genes are targets of RAR-RXR-activated pathways and increased by pro-vitamin A carotenoids, may contribute to a clearer picture of a possible interrelationship between dietary carotenoids, retinoids and atopy.

In summary, we found in our study that serum vitamin A and carotenoids from children at school age are not strongly related to atopy. The finding that a higher pro-vitamin A carotenoid serum level is associated with acculturation of Turkish migrant children in Germany leaves the possibility open that individual retinoids and/or carotenoids during initiation of allergic sensitization or other bioactive components alone or in combination with carotenoids present in food-stuff may be involved in protection or development of atopy. Subtle analysis of various dietary components in the serum, immune competent cells, skin or various target organs during the onset of atopy earlier in life remains an important issue in atopy research. Future studies should aim at the examination of birth cohorts of children and investigate a broader spectrum of relevant bioactive nutritional components in children and their mothers.

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