

Original article

Diet, serum fatty acids, and atopic diseases in childhood

Background: The reasons behind the reported increase in the occurrence of childhood atopic sensitization rates are unclear. We wanted to evaluate the association between dietary fats, serum fatty acids, and the occurrence and development of atopic diseases.

Methods: From a longitudinal database of a population-based sample, 231 sex- and age-matched pairs in 1980 and 154 pairs in 1986 were chosen, between whom we compared the dietary data, serum fatty acid composition, and occurrence of atopic diseases. The same variables were also compared between those who developed atopic disease later and those who did not during the 9-year follow-up.

Results: Examination of the dietary data in 1980 for those who had developed atopic disease compared with those who had remained healthy showed that the atopic children had used less butter before the expression of atopy. According to the cross-sectional data, the children with atopic disease consumed more margarine (mean 8.6 vs 7.3 [$P=0.04$]), and less butter (mean 9.4 vs 11.6 g/1000 kcal [$P=0.002$]), than the nonatopic children in 1980. Differences supporting these dietary findings were similarly found in the serum fatty acid data.

Conclusions: The diet of the atopic children differed from that of the nonatopic children in the consumption of polyunsaturated fat.

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Prevalence figures for atopic diseases vary widely from one country to another. High prevalence rates are reported in Australia and the UK and low rates in Eastern Europe and China (1–4). Likewise, an increase in the rates of hay fever and atopic sensitization in the former East Germany has been reported (1, 5, 6). Even though the increased occurrence of atopic diseases has not definitely been proven, it has been suggested that the Western diet with its increased intake of unsaturated fatty acids might be one triggering factor (3, 5–12). The consumption of polyunsaturated fatty acids may promote the formation of prostaglandin E_2 (PGE_2) by introducing a n-6 fatty acid, linoleic acid (c18:2), which is a precursor of arachidonic acid. PGE_2 is known to accelerate the formation of IgE from T cells. The polyunsaturated n-3 fatty acids eicosapentaenoic (EPA) and docosahexaenoic (DHA) found in fish oil competitively inhibit the formation of prostaglandins and leukotrienes derived from arachidonic acid, and they also have a suppressive effect on neutrophil function and thus an anti-inflammatory potential (13). A low consumption of oily fish has been found to be associated with an increased risk of asthma (14), although the addition of fish oil to the diet and the supplementation of eicosapentaenoic acid have failed to improve asthma (15–17).

We had access to a longitudinal database on atopic

diseases, the use of dietary fats, and measurements of serum fatty acids among a large population-based sample that made it possible to evaluate the association between dietary fats and the occurrence of atopic diseases during childhood and adolescence.

Material and methods

A multicenter survey of risk factors for coronary heart disease in Finland was started in 1980 and included a random sample of boys and girls aged 3, 6, 9, 12, 15, and 18 years from rural and urban areas (18). The number of subjects invited in 1980 was 4320; 3596 participated. The participants were invited to follow-up examinations 3 and 6 years later, the number of subjects participating in 1986 being 2799. Every other participant in 1980 was selected for complete dietary information collection and serum fatty acid measurement. The dietary survey was conducted altogether on 1768 children, and the fatty acid compositions of serum cholesterol esters were analyzed for 1348 children in 1980. The corresponding figures in 1986 were 732 and 759 (10). The dietary surveys were carried out by trained nutritionists using a 48-h recall method, and the intakes of dietary constituents were calculated from the food composition files of the Department of Nutrition, University of Helsinki. The serum fatty acid results were expressed as percentages of the total area of fatty acids from C14:0 to C22:6 as peaks in gas chromatography (19).

Questionnaires were completed by the parents in 1980 and checked by a nurse upon the parents returning them or when the children came for the physical examination. The questionnaire was repeated in 1983, 1986, 1989, and 1992, including, as in 1980, questions on asthma, allergic rhinitis, and atopic dermatitis diagnosed by a physician. Those children who had atopic diseases (atopic dermatitis,

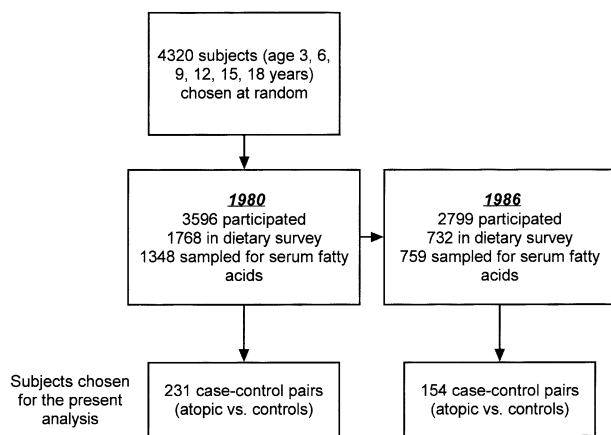


Figure 1. Flowchart of selection of case-control pairs for analysis.

allergic rhinitis, or asthma) and complete dietary data and serum fatty acid measurements served as the index cases, for whom age- and sex-matched controls were selected from among those with the same information available but no atopic diseases (Fig. 1). To minimize the effect of possible regional differences in the diagnosis of atopic diseases or in diet, the pairs were also matched by the place where they lived. The differences in the dietary composition and serum fatty acids between these case-control pairs with and without atopic diseases were tested with the paired-sample *t*-test. The total number of pairs was 231 in 1980 and 154 in 1986. The mean age of the pairs in 1980 was 10.3 years, and each group comprised 124 boys and 107 girls. The mean age of the boys was 9.8 years and that of the girls 10.9 years. The effect of fat intake, adjusted with respect to mother's education, on the occurrence of atopic disease was analyzed by logistic regression analysis for matched case-control data.

The dietary data in 1980 for the children who developed an atopic disease during the next 6 or 9 years were compared with the data for those who did not have atopic disease on any occasion by the means of the independent sample *t*-test. There were 84 new atopic children in 1986 and 60 in 1989, by comparison with 1288 and 1293 nonatopic children, respectively.

Results

Diet and atopy

The diet of the children with atopic dermatitis and allergic rhinitis in 1980 differed from that of the nonatopic children in the consumption of saturated and unsaturated fat standardized to energy intake (Table 1). The mean amount of margarine consumed by children with atopic dermatitis was 8.2 and that of butter 9.3 g/1000 kcal, as compared with 6.3 ($P=0.04$) and 11.5 g/1000 kcal ($P=0.03$) by the control group. The corresponding mean values among the children with allergic rhinitis and their controls were 9.9 vs 11.7 g/1000 kcal ($P=0.04$) for butter; for margarine, the difference was not statistically significant. The difference in the consumption of saturated and unsaturated fats was not significant in the comparison between the age- and sex-matched pairs in 1986. The children with atopic disease in 1980 consumed significantly more margarine ($P=0.04$) than the nonatopic children, and less butter (Table 2; $P=0.002$).

Table 1. Consumption of butter, margarine, and fish (as g/1000 kcal of energy intake) and dietary P/S ratio in 1980 in children with atopic dermatitis, allergic rhinitis, and asthma (cases) as compared with controls matched for age, sex, and place of residence

Variable	<i>n</i>	1980			
		Cases	Controls	Difference	
		Mean (SD)	Mean (SD)	<i>P</i> value	95% CI
Atopic dermatitis	124				
P/S ratio		0.24 (0.13)	0.20 (0.09)	0.01	0.01 to 0.07
Margarine		8.2 (6.9)	6.3 (6.2)	0.04	0.1 to 3.6
Butter		9.3 (8.5)	11.5 (7.5)	0.03	−4.1 to −0.2
Fish		5.9 (12.2)	7.5 (14.6)	0.34	−4.9 to 1.7
Allergic rhinitis	144				
P/S ratio		0.25 (0.15)	0.23 (0.12)	0.15	−0.01 to 0.06
Margarine		9.3 (7.3)	7.7 (6.9)	0.08	−0.2 to 3.2
Butter		9.9 (7.8)	11.7 (8.0)	0.04	−3.7 to −0.1
Fish		7.1 (15.3)	6.8 (13.6)	0.84	−2.9 to 3.6
Asthma	47				
P/S ratio		0.25 (0.12)	0.22 (0.12)	0.29	−0.01 to 0.07
Margarine		8.8 (7.4)	6.7 (5.4)	0.10	−0.4 to 4.6
Butter		9.2 (7.5)	10.4 (7.6)	0.34	−3.8 to 1.3
Fish		8.0 (20.1)	7.9 (14.4)	0.96	−7.0 to 7.3

The ratio of polyunsaturated to saturated fatty acids (P/S) was higher in the diet of the children with atopic dermatitis in 1980 than in controls (Table 1). In 1986, the corresponding value in children with atopic dermatitis compared to controls was 0.32 vs 0.27 ($P=0.03$). The P/S ratio was also higher among the children with atopic disease in 1980 (Table 2).

There was no difference in the consumption of fish when standardized to energy intake either among those with atopic disease or among those with atopic dermatitis, allergic rhinitis, or asthma separately (Tables 1 and 2).

Since the mother's education could be a confounding variable, we analyzed the effect of this by means of a logistic regression model. It did not affect the results.

Serum cholesteryl ester fatty acids and atopy

The percentage of myristic acid (c14:0) in the serum fatty acids was significantly lower in the children with atopic dermatitis in 1980 (Table 3). The fatty acids EPA (c20:5) and DHA (c22:6), which are found in fish, were lower in the children with atopic dermatitis in both 1980 (Table 3) and 1986. Their mean values for EPA were 0.91 in the children with atopic dermatitis vs 1.02 in the control group in 1986 ($P=0.02$), and those for DHA were 0.55 vs 0.61 ($P=0.01$) in 1986. There was no significant difference in serum linoleate (c18:2) in either 1980 (Table 3) or 1986.

Development of atopy

Examination of the dietary data in 1980 for those who had developed atopic disease by the year 1986 compared with those who stayed healthy showed that the atopic children had consumed less butter (mean 7.7

Table 2. Consumption of butter, margarine, and fish (as g/1000 kcal of energy intake) and P/S ratio and serum cholesteryl ester fatty acids in 1980 in children with atopic disease (atopic dermatitis, allergic rhinitis, or asthma; cases) as compared with controls matched for age, sex, and place of residence

		1980			
Variable	n	Cases	Controls	Difference	
		Mean (SD)	Mean (SD)	P value	95% CI
229					
P/S ratio		0.25 (0.13)	0.22 (0.11)	0.04	0.01 to 0.05
Margarine		8.6 (6.9)	7.3 (7.0)	0.04	0.8 to 2.6
Butter		9.4 (7.2)	11.6 (8.0)	0.002	−3.4 to −0.8
Fish		6.3 (13.8)	6.4 (12.6)	0.90	−2.6 to 2.3
231					
c18:2		51.00 (4.88)	50.83 (4.81)	0.68	−0.7 to 1.01
c14:0		0.97 (0.28)	0.99 (0.25)	0.39	−0.1 to 0.03
c20:5		1.18 (0.32)	1.22 (0.36)	0.22	−0.1 to 0.02
c22:6		0.65 (0.18)	0.68 (0.19)	0.09	−0.06 to 0.005

g/1000 kcal) than the nonatopic children (mean 10.1 g/1000 kcal [$P=0.001$]). The corresponding finding was seen also in 1989 (Table 4). The children with atopic diseases in 1989 had also consumed less fish in 1980 (mean 3.2 vs 6.6 g/1000 kcal [$P<0.001$]) (Table 4).

Discussion

Since the pivotal role of fat-derived inflammatory substances has been realized, the association between dietary fats and atopic disease has been increasingly investigated (14–17). Our finding that the atopic children consumed more margarine and less butter than nonatopic children supports the suggested importance of diet in the development of atopic disease among children (11, 12). The consumption of margarine, which is rich in n-6 polyunsaturated fatty acids, has been increasing over the past two decades in the Western diet. This is in accordance with the possible increase in the incidence and prevalence figures for atopic diseases, since the dietary changes which have taken place favor diets with more unsaturated fats and less dairy products in order to prevent cardiovascular diseases (1, 5, 9). This change in the dietary fats is thought to be one reason for the increasing prevalence of hay fever and atopy among children in the former East Germany after unification (6).

The dietary P/S ratio was significantly higher in the atopic children as a whole in 1980, and among the children with atopic dermatitis in both 1980 and 1986 (20, 21). We did not find any significant differences in the amount of serum linoleate (c18:2) between the atopic children and their controls, but serum myristic acid (c14:0) was significantly lower in the children with atopic dermatitis in 1980. Since high serum myristic acid has been found to be the best reflector of a high dietary intake of saturated fats (22), the low levels found in the children with atopic dermatitis may

Table 3. Serum cholesteryl ester fatty acids in children with atopic dermatitis, allergic rhinitis, or asthma (cases) as compared with age- and sex-matched controls living in same area in 1980

		1980			
Variable	n	Cases	Controls	Difference	
		Mean (SD)	Mean (SD)	P value	95% CI
Atopic dermatitis	126				
c18:2		51.53 (5.00)	51.30 (4.80)	0.68	−0.9 to 1.4
c14:0		0.93 (0.26)	1.01 (0.27)	0.02	−0.15 to −0.02
c20:5		1.11 (0.27)	1.22 (0.38)	0.01	−0.2 to −0.03
c22:6		0.64 (0.16)	0.69 (0.17)	0.01	−0.09 to −0.01
Allergic rhinitis	145				
c18:2		50.99 (4.87)	51.41 (4.74)	0.47	−1.5 to 0.7
c14:0		0.97 (0.27)	0.99 (0.26)	0.44	−0.1 to 0.04
c20:5		1.19 (0.32)	1.17 (0.35)	0.61	−0.1 to 0.1
c22:6		0.68 (0.18)	0.66 (0.17)	0.47	−0.02 to 0.1
Asthma	47				
c18:2		51.10 (4.71)	50.85 (4.46)	0.77	−1.4 to 1.9
c14:0		1.03 (0.30)	0.98 (0.27)	0.44	−0.1 to 0.2
c20:5		1.19 (0.31)	1.22 (0.32)	0.56	−0.2 to 0.1
c22:6		0.62 (0.17)	0.66 (0.14)	0.18	−0.1 to 0.02

indicate a lack of the protective effect of saturated fats against atopic diseases. Even though there was a difference between the atopic and healthy children in the consumption of margarine and butter in 1980, the difference of the same magnitude in 1986 was not statistically significant. This was due to the fact that there were fewer pairs in the comparison in 1986 and thus it had less statistical power.

The n-3 fatty acids EPA and DHA were significantly lower in the children with atopic dermatitis in both 1980 and 1986. This is in comparison with earlier findings in both children and adults with atopic dermatitis (23, 24). The dietary source of these fatty acids is fish, but we did not find any significant difference in the consumption of fish between the atopic and nonatopic children, although we did find that the consumption of fish was higher among those who remained healthy during the follow-up. EPA and DHA affect platelet aggregation and vasoconstriction, inhibit cellular growth factors and the migration of monocytes, and promote the synthesis of nitric oxide in the endothelium (25). The mechanisms by which they may prevent atopic sensitization are unknown, but the

Table 4. Dietary data (food consumption in g/1000 kcal) in 1980 of those who developed atopic disease in 1989 compared with those who remained healthy

Variable in 1980	Atopics (—89) Mean (SD)	Nonatopics (—89) Mean (SD)	Difference	
			P value	95% CI
n	60	1293		
Margarine	8.2 (6.7)	8.0 (7.4)	0.78	−2.0 to 1.5
Butter	8.3 (6.0)	10.2 (7.8)	0.02	0.27 to 3.4
Fish	3.2 (6.5)	6.6 (13.0)	<0.001	1.6 to 5.2
P/S ratio	0.24 (0.11)	0.24 (0.13)	0.73	−0.04 to 0.03

n: number of children participating in dietary survey in 1980.

low prevalence rate of asthma among the Inuit, who consume large amounts of fish and thus EPA from fish oil, parallels our results regarding the importance of the quality of the fat consumed (26). In a study of the anti-inflammatory effects of EPA and DHA supplementation on mild asthmatics, a 50% inhibition of total leukotriene B from neutrophils and suppressed neutrophil chemotaxis was found, but there was no change in clinical measures of the disease (14). In a randomized trial of school-aged children, the dietary enrichment of n-3 fatty acids did increase the plasma levels of these fatty acids and reduced stimulated tumor necrosis factor- α production but had no effect on the clinical severity of asthma (17). This could mean that subjects with too little EPA and DHA in their diet run

an increased risk of developing atopy, but that an excess of these fatty acids does not prevent its development.

Our results support the hypothesis that the quality of the fat consumed in the diet is important for the development of atopic diseases in children. The possibility of preventing atopic diseases by supplementation or by changing the fatty acid composition of the diet of young children remains to be tested by clinical trials.

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