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Fatty acid intake and asthma symptoms in Japanese children: The Ryukyus Child Health Study

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Clinical and Experimental Allergy

Summary

Background It has been hypothesized that increased consumption of n-6 polyunsaturated fatty acids and decreased consumption of n-3 polyunsaturated fatty acids have contributed to the recent increased prevalence of asthma.

Objectives The present cross-sectional study examined the association of intake of specific types of fatty acids with the prevalence of asthma symptoms using data from the Ryukyus Child Health Study.

Methods Study subjects were 25 033 schoolchildren aged 6–15 years in Okinawa, Japan. Symptoms of wheeze and asthma were defined according to diagnostic criteria from the International Study of Asthma and Allergies in Childhood. Information on dietary factors was collected using a self-administered brief diet history questionnaire for children. Adjustment was made for age, sex, number of siblings, smoking in the household, body mass index, paternal and maternal history of allergic diseases, and paternal and maternal educational level.

Results Intake of polyunsaturated fatty acids, n-3 and n-6 polyunsaturated fatty acids and linoleic acid (18 : 2 n-6) was independently associated with an increased prevalence of wheeze – the multivariate odds ratios for the highest quintile were 1.19 (95% confidence interval [CI], 1.05–1.35), 1.17 (95% CI, 1.03–1.34), 1.19 (95% CI, 1.04–1.35), and 1.20 (95% CI, 1.06–1.37), respectively. There was no measurable relationship of consumption of α -linolenic (18 : 3 n-3), eicosapentaenoic (20 : 5 n-3), docosahexaenoic (22 : 6 n-3) or arachidonic acid (20 : 4 n-6) or the ratio of n-3 to n-6 polyunsaturated fatty acids with the prevalence of wheeze.

Consumption of total fat, saturated fatty acids, monounsaturated fatty acids and cholesterol were not evidently related to wheeze. No material dose–response association was found between the intake of any of the types of fatty acids considered and the prevalence of asthma.

Conclusions The findings suggest that consumption of both n-3 and n-6 polyunsaturated fatty acids, especially linoleic acid, may be associated with an increased prevalence of wheeze.

Keywords asthma, intake, Japanese children, linoleic acid, n-3 polyunsaturated fatty acids, n-6 polyunsaturated fatty acids, wheeze

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Introduction

Over the last few decades, the prevalence of childhood asthma has increased in Japan as well as in Western countries [1]. The rapid increase in the prevalence of asthma is not likely to be explained by genetic shifts. Thus, epidemiological research has paid attention to

environmental factors. The Westernization of lifestyle over this time period has been proposed as a potential explanation for the observed increase. In particular, change in eating habits may influence the development of asthma in developed countries. One study of Japanese male adults in a rural area showed a decrease in the intake of carbohydrates from 84% in 1958 to 62% in 1999 and an

increase in intake of fat from 5% to 20%, protein from 11% to 18%, fish from 56 to 71 g/day and meat from 13 to 92 g/day, from 1958 to 1999 [2].

It has been hypothesized that increased consumption of n-6 polyunsaturated fatty acids and decreased consumption of n-3 polyunsaturated fatty acids have contributed to the recent increases in the prevalence of asthma [3]. However, epidemiological evidence is scarce in children. A cross-sectional study in Australian pre-school children showed a significant positive association between polyunsaturated fats on bread and in cooking, and the prevalence of asthma [4]. A higher ratio of n-6- to n-3 polyunsaturated fatty acid intake was significantly associated with an increased risk of current asthma in a nested case-control study among Australian children [5]. A significant inverse relationship between oily fish intake and childhood asthma was observed in Australia [6]. Intake of bread and margarine was significantly positively related to the prevalence of wheeze whereas no association with fish intake was found in a cross-sectional study among Italian children [7]. A positive association between fish intake and the prevalence of asthma was demonstrated among Japanese children [8]. Some of these findings may support that hypothesis, at least regarding the detrimental effect of n-6 polyunsaturated fatty acid intake on asthma. However, the evidence is insufficient to implicate polyunsaturated fatty acids as risk or preventive factors for asthma. This is partially due to limited but inconsistent findings, differences in definitions of asthma and methodological deficiencies in studies conducted to date.

In view of the lack of epidemiological information regarding a relationship between polyunsaturated fatty acid intake and asthma in Japanese children, we examined the association of intake of specific types of fatty acids with the prevalence of asthma symptoms using data from the Ryukyus Child Health Study (RYUCHS).

Methods

Study population

Okinawa Prefecture is an island located in the southernmost area in Japan, with a subtropical climate and a total population of almost 1 370 000. Naha City, the largest city in Okinawa Prefecture and located in the south of the island, and Nago City, located in the centre of the island, with a total population of almost 313 000 and 60 000, respectively, are 2 of the 41 municipalities in Okinawa Prefecture. All 35 public elementary schools and 17 junior high schools in Naha City and 17 public elementary schools and eight junior high schools in Nago City participated in the RYUCHS during the period from September 2004 to January 2005. The RYUCHS was a cross-sectional survey that investigated the associations between various selected factors and child health problems. A set of two self-administered questionnaires was

distributed by teachers to all 38 212 schoolchildren aged 6–15 years. The questionnaires were answered by the parents of the elementary schoolchildren and the junior high school students themselves and/or their parents. When research technicians found missing or illogical data, the teachers sent the questionnaires back to the parents. The RYUCHS was approved by the ethics committee of the Faculty of Medicine, Fukuoka University.

Measurements

One of the self-administered questionnaires included questions on asthma symptoms in the past 12 months based on the validated criteria of the International Study of Asthma and Allergies in Childhood Phase One study. We translated these questions into Japanese by using standard forward-backward translation. Wheeze was defined as positive if the children or their parents answered 'yes' to the written question 'Have you (Has your child) had wheezing or whistling in the chest in the last 12 months?' Those children who responded positively to both the aforementioned question and a second question, 'Have you (Has your child) ever had asthma?', were considered to have asthma. The questionnaire also yielded information on age, sex, number of siblings, smoking in the household, paternal and maternal history of asthma, atopic eczema and allergic rhinitis, and paternal and maternal educational level. A paternal or maternal history of allergic diseases was defined as positive if the respective parent had contracted asthma, atopic eczema and/or allergic rhinitis before the start of the survey.

Dietary habits over a period of 1 month were assessed using the other instrument, which was a self-administered brief diet history questionnaire (BDHQ) for children. This instrument enquires about the consumption frequency of 51 selected food and non-alcoholic beverage items commonly consumed in the general population of Japanese children, with specified serving sizes described in terms of either the common unit, weight or volume of each serving. The BDHQ for children was developed based on a comprehensive version of a validated self-administered diet history questionnaire [9–11]. Estimates of dietary intake of 51 food and beverage items as well as energy and nutrients were calculated using an *ad hoc* computer algorithm for the BDHQ for children, which was based on the Standard Tables of Food Composition in Japan [12, 13]. Energy-adjusted intake by the residual approach was used for the analyses [14]. The BDHQ also inquired about weight and height of the child. Body mass index was calculated by dividing self-reported body weight (kg) by the square of self-reported height (m²).

Statistical analysis

Intake of selected nutrients was categorized at quintile points on the basis of the distribution of all study subjects.

Age, sex, residential municipality, number of siblings, smoking in the household, body mass index, paternal and maternal history of allergic diseases, and paternal and maternal educational level were selected *a priori* as potential confounding factors. Age was classified into three categories (6–8, 9–11 and 12–15 years), number of siblings into four (0, 1, 2 and 3+), smoking in the household into three (never, former and current), and paternal and maternal educational level into four (junior high school, high school, junior college or vocational technical school, and university). Body mass index was used as a continuous variable. Logistic regression analysis was used to compare the prevalence of asthma symptoms with the intake of specific types of fatty acids. Also, multiple logistic regression analysis was used to control for the potential confounding factors under investigation. Trend of association was assessed by a logistic regression model assigning consecutive integers to the levels of the independent variable. Two-sided *P*-values less than 0.05 were regarded as statistically significant. All computations were performed using the SAS software package, version 9.1 (SAS Institute, Inc., Cary, NC).

Results

Of the 38 212 eligible subjects, 28 885 children (75.6%) participated in the RYUCHS. Excluded were 3852 children because of missing or illogical data on the factors under investigation, leaving 25 033 subjects (65.5%) for analysis. Compared with the 3852 participants, the 25 033 study subjects were less likely to have no siblings, have former smokers in the household, and have mothers with a history of asthma and atopic eczema, and were more likely to be male and young, report a paternal history of allergic rhinitis, have both fathers and mothers with a high educational level, have a high intake of n-3 and n-6 polyunsaturated fatty acids (data not shown). There was no substantial difference between the excluded participants and study subjects regarding the prevalence of wheeze and asthma, a paternal history of asthma and atopic eczema, and a maternal history of allergic rhinitis.

The prevalence values for symptoms of wheeze and asthma in the previous 12 months were 10.8% and 7.7%, respectively, among 25 033 children. Many more children had parents with a history of allergic rhinitis than parents with a history of asthma or atopic eczema (Table 1). Mean daily energy-adjusted n-3 and n-6 polyunsaturated fatty acid consumptions were 2.1 and 10.3 g, respectively.

Odds ratios (ORs) and their 95% confidence intervals (CIs) for the prevalence of wheeze and asthma in relation to dietary intake of polyunsaturated fatty acids are provided in Table 2. Both a positive dose–response relationship between polyunsaturated fatty acid intake and the

Table 1. Distribution of selected characteristics in 25 033 schoolchildren, Ryukyus Child Health Study (RYUCHS), Japan

Variable	No. (%) or mean (SD)
Age (years)	
6–8	7457 (29.8)
9–11	9032 (36.1)
12–15	8544 (34.1)
Male sex	12 356 (49.4)
Municipality	
Naha City	20 567 (82.2)
Nago City	4466 (17.8)
Siblings	
0	2305 (9.2)
1	8421 (33.6)
2	9455 (37.8)
3+	4852 (19.4)
Smoking in household	
Never	10 780 (43.1)
Former	2570 (10.3)
Current	11 683 (46.7)
Paternal history of allergic diseases*	5893 (23.5)
Maternal history of allergic diseases*	7085 (28.3)
Paternal educational level	
Junior high school	1946 (7.8)
High school	11 115 (44.4)
Junior college or vocational technical school	3709 (14.8)
University	8263 (33.0)
Maternal educational level	
Junior high school	1256 (5.0)
High school	11 085 (44.3)
Junior college or vocational technical school	10 431 (41.7)
University	2261 (9.0)
Body mass index (kg/m ²)	17.8 (3.1)
Daily nutrient intake [†]	
Total energy (kJ)	8426 (2412)
Total fat (g)	66.7 (12.2)
Saturated fatty acids (g)	2.3 (0.5)
Monounsaturated fatty acids (g)	21.4 (4.5)
Polyunsaturated fatty acids (g)	14.4 (3.1)
n-3 Polyunsaturated fatty acids (g)	2.1 (0.6)
n-6 Polyunsaturated fatty acids (g)	10.3 (2.8)
Cholesterol (mg)	402.1 (119.3)

* Asthma, atopic eczema or allergic rhinitis.

[†] Nutrient intake was adjusted for total energy intake using the residual method [14].

prevalence of wheeze and the crude OR for comparison of the highest with the lowest quintile reached statistical significance. After adjustment for age, sex, residential municipality, number of siblings, smoking in the household, body mass index, paternal and maternal history of allergic diseases, and paternal and maternal educational level, the positive relationship remained significant, albeit slightly attenuated. No measurable association was found between the consumption of polyunsaturated fatty acids and the prevalence of asthma in the multivariate model.

Table 2. Odds ratios (ORs) and 95% confidence intervals (CIs) for asthma symptoms in relation to dietary intake of polyunsaturated fatty acids in 25 033 schoolchildren, Ryukyus Child Health Study (RYUCHS), Japan

Variable*	Wheeze			Asthma		
	Prevalence (%)	Crude OR (95% CI)	Adjusted OR (95% CI) [†]	Prevalence (%)	Crude OR (95% CI)	Adjusted OR (95% CI) [†]
Polyunsaturated fatty acids						
Q1 (10.8)	10.0	1.00	1.00	7.1	1.00	1.00
Q2 (12.9)	10.8	1.10 (0.96–1.25)	1.09 (0.96–1.24)	7.8	1.11 (0.96–1.29)	1.11 (0.95–1.29)
Q3 (14.3)	11.0	1.12 (0.99–1.28)	1.10 (0.97–1.25)	7.9	1.12 (0.97–1.30)	1.11 (0.95–1.29)
Q4 (15.7)	10.6	1.07 (0.94–1.22)	1.04 (0.91–1.18)	7.7	1.09 (0.94–1.27)	1.06 (0.91–1.24)
Q5 (18.1)	11.8	1.22 (1.07–1.38)	1.19 (1.05–1.35)	8.1	1.16 (1.00–1.35)	1.13 (0.97–1.32)
<i>P</i> for trend		0.01	0.04		0.10	0.25
n-3 Polyunsaturated fatty acids						
Q1 (1.3)	9.8	1.00	1.00	7.0	1.00	1.00
Q2 (1.7)	11.5	1.20 (1.05–1.36)	1.20 (1.05–1.36)	8.4	1.22 (1.05–1.42)	1.23 (1.06–1.43)
Q3 (2.0)	10.7	1.10 (0.96–1.25)	1.08 (0.95–1.23)	7.6	1.09 (0.94–1.27)	1.08 (0.93–1.26)
Q4 (2.3)	10.7	1.09 (0.96–1.24)	1.06 (0.93–1.21)	7.6	1.10 (0.95–1.28)	1.08 (0.92–1.26)
Q5 (2.8)	11.5	1.20 (1.05–1.36)	1.17 (1.03–1.34)	7.9	1.14 (0.98–1.33)	1.12 (0.96–1.31)
<i>P</i> for trend		0.07	0.18		0.37	0.62
α -Linolenic acid (18 : 3 n-3)						
Q1 (0.8)	10.2	1.00	1.00	7.1	1.00	1.00
Q2 (1.2)	10.3	1.02 (0.89–1.16)	1.01 (0.89–1.15)	7.5	1.06 (0.91–1.23)	1.06 (0.91–1.24)
Q3 (1.5)	11.1	1.10 (0.97–1.25)	1.07 (0.94–1.22)	7.9	1.13 (0.97–1.31)	1.11 (0.96–1.29)
Q4 (1.8)	11.2	1.12 (0.98–1.27)	1.08 (0.95–1.23)	8.0	1.14 (0.99–1.33)	1.12 (0.96–1.30)
Q5 (2.4)	11.4	1.14 (1.01–1.30)	1.11 (0.98–1.26)	7.9	1.13 (0.97–1.31)	1.10 (0.94–1.28)
<i>P</i> for trend		0.01	0.06		0.06	0.17
Eicosapentaenoic acid (20 : 5 n-3)						
Q1 (0.03)	11.1	1.00	1.00	7.8	1.00	1.00
Q2 (0.06)	10.7	0.96 (0.85–1.09)	0.98 (0.86–1.11)	7.6	0.96 (0.83–1.12)	0.99 (0.85–1.15)
Q3 (0.09)	10.6	0.95 (0.84–1.08)	0.96 (0.84–1.09)	7.6	0.97 (0.84–1.13)	0.99 (0.85–1.15)
Q4 (0.11)	10.4	0.94 (0.82–1.06)	0.95 (0.83–1.08)	7.4	0.94 (0.81–1.09)	0.96 (0.82–1.11)
Q5 (0.22)	11.5	1.04 (0.92–1.18)	1.05 (0.93–1.20)	8.0	1.03 (0.89–1.19)	1.04 (0.90–1.21)
<i>P</i> for trend		0.67	0.58		0.87	0.76
Docosahexaenoic acid (22 : 6 n-3)						
Q1 (0.11)	10.9	1.00	1.00	7.7	1.00	1.00
Q2 (0.18)	10.6	0.97 (0.85–1.10)	0.99 (0.87–1.12)	7.6	0.98 (0.85–1.14)	1.02 (0.87–1.18)
Q3 (0.23)	10.5	0.96 (0.85–1.09)	0.96 (0.84–1.09)	7.4	0.95 (0.82–1.10)	0.95 (0.82–1.10)
Q4 (0.30)	11.1	1.03 (0.90–1.16)	1.04 (0.92–1.18)	8.2	1.06 (0.92–1.22)	1.08 (0.94–1.26)
Q5 (0.47)	11.0	1.01 (0.90–1.15)	1.03 (0.91–1.17)	7.6	0.98 (0.85–1.14)	1.00 (0.86–1.16)
<i>P</i> for trend		0.54	0.42		0.83	0.68
n-6 Polyunsaturated fatty acids						
Q1 (7.1)	10.1	1.00	1.00	7.1	1.00	1.00
Q2 (8.9)	10.7	1.07 (0.94–1.21)	1.06 (0.93–1.21)	7.7	1.09 (0.94–1.27)	1.09 (0.94–1.27)
Q3 (10.2)	10.9	1.09 (0.96–1.24)	1.07 (0.94–1.22)	7.8	1.10 (0.95–1.28)	1.09 (0.93–1.27)
Q4 (11.4)	10.8	1.08 (0.95–1.23)	1.05 (0.92–1.20)	7.9	1.12 (0.97–1.30)	1.10 (0.95–1.28)
Q5 (13.6)	11.9	1.21 (1.07–1.37)	1.19 (1.04–1.35)	8.0	1.14 (0.99–1.33)	1.13 (0.97–1.31)
<i>P</i> for trend		0.006	0.02		0.08	0.15
Linoleic acid (18 : 2 n-6)						
Q1 (5.7)	10.1	1.00	1.00	7.1	1.00	1.00
Q2 (7.9)	10.6	1.06 (0.94–1.21)	1.06 (0.93–1.21)	7.7	1.08 (0.93–1.26)	1.08 (0.93–1.26)
Q3 (9.6)	11.0	1.10 (0.97–1.25)	1.08 (0.95–1.23)	7.8	1.11 (0.96–1.29)	1.10 (0.94–1.28)
Q4 (11.6)	10.5	1.05 (0.93–1.20)	1.03 (0.90–1.17)	7.7	1.08 (0.93–1.26)	1.06 (0.91–1.23)
Q5 (14.9)	12.0	1.22 (1.08–1.39)	1.20 (1.06–1.37)	8.2	1.17 (1.01–1.35)	1.15 (0.99–1.33)
<i>P</i> for trend		0.006	0.02		0.07	0.14
Arachidonic acid (20 : 4 n-6)						
Q1 (0.06)	10.9	1.00	1.00	7.8	1.00	1.00
Q2 (0.09)	9.9	0.90 (0.79–1.02)	0.90 (0.79–1.02)	6.9	0.87 (0.75–1.01)	0.87 (0.75–1.01)
Q3 (0.12)	11.9	1.10 (0.97–1.24)	1.09 (0.96–1.23)	8.5	1.09 (0.94–1.26)	1.08 (0.94–1.25)
Q4 (0.15)	10.8	0.99 (0.87–1.12)	0.98 (0.86–1.12)	7.8	0.99 (0.86–1.15)	1.00 (0.86–1.16)

Table 2. continued

Variable*	Wheeze			Asthma		
	Prevalence (%)	Crude OR (95% CI)	Adjusted OR (95% CI) [†]	Prevalence (%)	Crude OR (95% CI)	Adjusted OR (95% CI) [†]
Q5 (0.18)	10.7	0.98 (0.87–1.12)	0.99 (0.87–1.13)	7.5	0.95 (0.82–1.10)	0.96 (0.83–1.12)
<i>P</i> for trend		0.71	0.62		0.87	0.74
n-3/n-6 Polyunsaturated fatty acid ratio						
Q1 (0.17)	10.8	1.00	1.00	7.5	1.00	1.00
Q2 (0.18)	10.9	1.01 (0.89–1.15)	1.01 (0.88–1.14)	7.6	1.02 (0.88–1.19)	1.02 (0.88–1.18)
Q3 (0.20)	11.6	1.08 (0.96–1.23)	1.06 (0.93–1.20)	8.3	1.11 (0.96–1.29)	1.09 (0.94–1.27)
Q4 (0.21)	10.1	0.93 (0.82–1.06)	0.89 (0.78–1.02)	7.4	0.99 (0.86–1.15)	0.95 (0.82–1.11)
Q5 (0.23)	10.8	1.00 (0.88–1.14)	0.99 (0.87–1.13)	7.7	1.03 (0.89–1.19)	1.01 (0.87–1.18)
<i>P</i> for trend		0.57	0.36		0.90	0.81

*Quintile medians in g/day adjusted energy intake using the residual method are given in parentheses, except for the ratio of n-3 to n-6 polyunsaturated fatty acids, which was based on crude intake in g/day.

[†]Adjustment for age, sex, residential municipality, number of siblings, smoking in the household, body mass index, paternal and maternal history of allergic diseases, and paternal and maternal educational level.

Compared with n-3 polyunsaturated fatty acid intake in the first quintile, its consumption in the second and fifth quintiles was significantly associated with an increased prevalence of wheeze although the linear trend was not statistically significant after multivariate adjustment. A significant positive association of n-3 polyunsaturated fatty acid intake with the prevalence of asthma was found only when comparing the second with the first quintile after controlling for confounders. There was no evident relationship between the intake of α -linolenic, eicosapentaenoic or docosahexaenoic acid and wheeze or asthma in the multivariate model. Consumption of n-6 polyunsaturated fatty acids in the highest quintile was independently associated with an increased prevalence of wheeze, and the positive linear trend was statistically significant after multivariate adjustment (*P* for trend = 0.02). No such relationship was noted for asthma in the multivariate model. Intake of linoleic acid was independently related to an increased prevalence of wheeze after allowance for confounding factors: the adjusted OR for comparing the highest with the lowest quintile was 1.20 (95% CI, 1.06–1.37, *P* for trend = 0.02). For the prevalence of asthma, the OR for linoleic acid consumption in the highest quintile was not statistically significant in the multivariate analysis. Neither arachidonic acid intake nor the ratio of n-3 to n-6 polyunsaturated fatty acids was associated with the prevalence of wheeze or asthma.

Intake of total fat, saturated fatty acids, monounsaturated fatty acids or cholesterol was not measurably related to either outcome (data not shown). However, a significant inverse association was found between saturated fatty acid intake in the fourth quintile and asthma by the multivariate model: the adjusted OR was 0.85 (95% CI, 0.73–0.99, *P* for trend = 0.16).

Discussion

Strengths and limitations

The current study had methodological advantages in that the prevalence of symptoms of wheeze and asthma was estimated by validated core questions in the International Study of Asthma and Allergies in Childhood Phase One study and that study subjects were homogeneous in terms of age and geographical background. The extensive information on potential confounding factors and the large study size allowed us to examine confounding in detail. However, this study did not include data on allergen exposure and the home environment, which is a major weakness. There are inherent limitations to the accuracy of the self-administered BDHQ for children. The validity of the BDHQ for children was not assessed although the BDHQ for children was developed based on the BDHQ for adults, which was in turn developed based on a well-validated, self-administered, comprehensive diet history questionnaire for adults [9–11]. However, the validity of the BDHQ for adults appears reasonable. The Pearson correlation coefficients between intake assessed using the BDHQ for adults and by a 16-day weighed dietary record in 92 men and 92 women were 0.38 and 0.40 for polyunsaturated fatty acids. The intake of eicosapentaenoic and docosahexaenoic acids obtained from the BDHQ for adults significantly positively correlated with serum concentrations of eicosapentaenoic and docosahexaenoic acids (unpublished observations, Sasaki, 2004). However, questions about the validity of the BDHQ for children are reasonable, although a dietary questionnaire developed for children based on a validated questionnaire for adults appears to provide reasonable estimates of dietary intake [15]. Our dietary assessment may have been insufficient to

allow the detection of true associations between dietary factors and the outcomes under study. It is unclear whether the estimates of specific types of fatty acids derived from the BDHQ for children reflect long-term intake by study subjects. Nevertheless, patients with asthma were not likely to be aware of the ill effects of diet. The consequence would have given rise to an underestimation of our results.

Other weaknesses should also be considered. Selection bias might be inevitable because only 65.5% of the eligible subjects were included in the current analysis. Study subjects may be different from Japanese children in the general population. The prevalence of wheeze in Okinawa may be higher than that in the mainland of Japan. Using the same criteria as used in this study, the prevalence value for wheeze symptoms in the past 12 months was 6.7% among adolescents in Suita City, an urban city on the mainland [16]. Thus, we should be cautious in generalizing the present observations.

Comparison with other studies

There is some available epidemiological evidence in adults with regard to the relationship between dietary polyunsaturated fatty acid intake and asthma symptoms. The Nurses' Health Study found that a comparison of the highest and the lowest quintile of intake of linoleic acid, but not n-3 polyunsaturated fatty acids, resulted in a significant inverse association with the risk of asthma [17]. Intake of linoleic acid, arachidonic acid, α -linolenic acid, eicosapentaenoic acid, and docosahexaenoic acid and the n-6/n-3 polyunsaturated fatty acid ratio were unrelated to the risk of asthma in a nested case-control study within a prospective study in Germany [18]. Another case-control study in Spain showed no statistical differences in the intake of n-3 or n-6 polyunsaturated fatty acids and the n-6/n-3 ratio between asthmatic and non-asthmatic subjects [19]. In a cross-sectional study of Australian young adults using plasma fatty acid levels, no material associations were found between any of the n-3 series polyunsaturated fatty acids, linoleic acid, arachidonic acid, total n-3 polyunsaturated fatty acids, total n-6 polyunsaturated fatty acids or the n-6/n-3 ratio and asthma outcomes although dihomogamma-linolenic acid (20:3 n-6) was positively associated with asthma [20]. A Japanese cross-sectional study demonstrated that the intake of n-3 and n-6 polyunsaturated fatty acids was not related to the prevalence of asthma although a significant inverse relationship was observed between the ratio of n-3 to n-6 polyunsaturated fatty acid intake and the prevalence of asthma among pregnant women [21]. The current results are in partial agreement with these observations. Also, the present findings are partially consistent with the results of a previous epidemiological

study among children that showed a positive association between the intake of bread and margarine and the prevalence of wheeze and no relationship between fish intake and wheeze [7]. The difference in eating habits between countries or regions might lead to inconsistent findings.

Implications of the study

Linoleic acid is converted into arachidonic acid that can be metabolized by cyclooxygenase and lipoxygenase enzymes ultimately to produce two-series prostaglandins and thromboxanes and four-series leukotrienes and lipoxins, which are of particular pertinence to asthma [22]. Prostaglandin E_2 and leukotriene B_4 have pro-inflammatory biological actions [23]. Prostaglandin E_2 influences the T-helper cell type 1 to T-helper cell type 2 ratios and subsequently inhibits interferon- γ production, with no effect on interleukin-4, thus stimulating immunoglobulin E synthesis [24]. An increase in the amount of linoleic acid in the diet may have resulted in increased prostaglandin E_2 production, with a consequent increase in wheeze in our findings. Linoleic acid consumption was not independently related to the prevalence of asthma in the present study, however.

In contrast, α -linolenic acid competitively inhibits linoleic acid metabolism by the single enzyme cascade [22]. The present study population was consuming very high amounts of n-3 polyunsaturated fatty acids. In a nested case-control study among Australian children showing a significant positive association between the ratio of n-6 to n-3 fatty acids in the diet and the risk of asthma [5], the mean values of daily n-3 polyunsaturated fatty acid intake and the ratio of n-3 to n-6 polyunsaturated fatty acid intake among 169 controls were 1.05 g and 0.065, respectively; these values were much lower than the corresponding figures in this study (2.05 g and 0.199, respectively). Thus, a preventive relationship of n-3 polyunsaturated fatty acid intake and the ratio of n-3 to n-6 fatty acid intake to asthma may be substantiated when consumption of n-3 polyunsaturated fatty acids is very low. However, a high ratio of n-3 to n-6 polyunsaturated fatty acid intake was associated with a reduced prevalence of asthma in female Japanese young adults in a previously cited paper [21]. In Japan, intake of fish is high. Unknown active substances in fish might have interfered with the benefit of marine origin n-3 polyunsaturated fatty acids on asthma symptoms. For example, methylmercury and dioxins are accumulated in fish and shellfish through the marine food web. A systematic review of controlled clinical trials by the Cochrane Collaboration concluded that there is little evidence to recommend that patients with asthma supplement or modify their dietary intake of n-3 fatty acids in the management of asthma [25].

Conclusion

This report is the first epidemiological study on the intake of specific types of fatty acids and asthma symptoms in Japanese children. However, the current cross-sectional study cannot demonstrate a cause and effect relationship for the associations under study. Lack of dose-response relationships between dietary factors under study and the prevalence of asthma may be ascribed to the possible influence of reserve causation: asthma patients might have had healthy eating habits. Further investigations, especially prospective studies, are needed to clarify these associations.

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