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Letter to the Editor

Food-dependent exercise-induced anaphylaxis among junior high school students: A 14-year epidemiological comparison

Dear Editors

Food-dependent exercise-induced anaphylaxis (FEIAn) is a distinct type of allergy provoked by a combination of specific food ingestion and physical exercise. We found that the morbidity of FEIAn in junior-high-school students in Yokohama 14 years ago was 0.017% and that only 30% of junior-high-school nurses were aware of this condition.¹ No large-scale epidemiological studies have been implemented thereafter. We performed an epidemiological study similar to the previous one to compare the present morbidity, school-nurses' familiarity with FEIAn and measures to prevent recurrence at schools with those determined 14 years previously.

We mailed a survey to all nurses at 148 public junior-high-schools in Yokohama in November 2012 with the permission of the Board of Education. The survey included questions about the number of students, their knowledge of FEIAn, the number of students with FEIAn, and their detailed information. Then, we directly contacted nurses to confirm their responses. We considered a student as having FEIAn when the following criteria from the previous study¹ were fulfilled: (1) symptoms provoked by physical exercise after ingesting a specific food, but not provoked by either food or exercise alone and (2) symptoms involving more than two organs; however cutaneous symptoms could include only severe symptoms such as generalized urticaria or angioedema of the face. A food item was considered as the suspected causative agent on the basis of the following criteria: positive diagnostic findings with skin prick tests, Immuno CAP system (Phadia AB, Uppsala, Sweden) and provocation tests, and prevention of recurrence after strict elimination of suspected foods before exercise. Data from two studies were compared and statistically analyzed using the χ^2 test or Fisher's exact test. A P value <0.05 was considered to represent a statistically significant difference. The institutional review board at the Kanagawa Prefectural Ashigarakami Hospital approved the study.

This study included data from 76,534 students (39,767 boys and 36,767 girls). Reports from school nurses indicated that 35 students had FEIAn. However, 20 students who did not meet the criteria were excluded. We also excluded one student who developed anaphylaxis after eating a wheat product followed by exercise, because he had previously undergone oral immunotherapy (OIT) for wheat allergy. This student had been eating wheat without limitations. The remaining 14 (7 boys and 7 girls) were deemed to have FEIAn.

The morbidity of FEIAn was 0.018%. Eleven (78.6%) students experienced a first episode of FEIAn after 9 years of age. Six (42.9%) had other allergic disorders, four had allergic rhinitis and one each had food allergy, atopic dermatitis and allergic conjunctivitis. The causative foods among the 14 students were crustaceans (n = 5), wheat (n = 4), and unknown (n = 5, two suspected crustaceans). All students already had been clinically diagnosed with FEIAn at the time of this study. Of the 9 students in whom the causative food was identified, two were confirmed by provocation tests.

Nine (64.3%) of them had experienced several FEIAn episodes and three of them had experienced over five episodes.

Measures taken to prevent recurrence consisted of restricting the causative food or exercise in 13 (93%) of the students. Seven of them were prescribed oral medications including antihistamines and five carried an adrenaline auto-injector. Among 141 school nurses, 43 (30.5%) had reasonable knowledge of FEIAn and 83 (58.9%) had a little information.

The present findings indicated that morbidity rates and causative foods have not remarkably changed over 14 years and that recurrence rates remained high, despite the fact that school nurses had a better understanding of FEIAn (Table 1). Although we estimated an increase in the FEIAn morbidity, rates did not significantly differ between the previous and the present study (0.017% vs. 0.018%). The major causative foods remained crustaceans and wheat. However, only four (30.7%) of 13 students had been diagnosed with FEIAn in the previous study, whereas all were diagnosed in the present study. This difference reflects the fact that the medical establishment has also become more knowledgeable about FEIAn over the past 14 years.

Approximately 90% of school nurses had at least heard of FEIAn compared with 32% in the previous study. However, their level of understanding of FEIAn was insufficient and they had not collected precise information from students.

Only 30% of schools that had students with FEIAn had previously implemented some measures to prevent recurrence, and approximately 35% of schools did not know how to implement these safeguards. In contrast, in the present study, most schools had made efforts to prevent recurrence. However, 64.3% of students still experienced several FEIAn episodes. This indicated that the improved knowledge among school nurses and precautionary steps taken in schools were insufficient to prevent recurrence.

Defining the causative food in the medical setting might be neither easy nor sufficient. The development of FEIAn has been associated with several risk factors, such as physical status, exercise intensity, weather, amount of intake, combinations of foods, and some drugs.^{2–4} Therefore, allergic reactions are not always

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Table 1
Comparison between present and previous studies.

Study period	1998	2012	P
Collection rate (%)	132/145 (91.0)	141/148 (95.2)	P = 0.15 [†]
Morbidity (%)	13/76,247 (0.017)	14/76,534 (0.018)	P = 0.86 [†]
Boys/Girls	11/2	7/7	P = 0.07 [†]
Suspected foods (number)	Crustaceans (7) Wheat (4) Fruits (1) Vegetables (1) Buckwheat (1) Unknown (2)	Crustaceans (5) Wheat (4) Unknown (5)	
Diagnostic rate (%)	4/13 (30.8)	14/14 (100)	P < 0.001 [‡]
Precautions implemented in schools (%) [§]	4/13 (30.8)	13/14 (92.8)	P = 0.001 [‡]
Recurrence (%) [¶]	10/13 (76.9)	9/14 (64.3)	P = 0.39 [†]
Familiarity of school nurses (%)	16/50 (32.0)	126/141 (89.4)	P < 0.001 [†]

[†] χ^2 test.

[‡] Fisher's exact test.

[§] restricted causative food or exercise.

[¶] experienced several anaphylactic episodes.

triggered by provocation tests. However, the causative food remained undetermined in one-third of affected students in the present study. Other reasons for frequent recurrence might be insufficient investigation after the first episode and insufficient education about FEIAn to students and their parents in the medical setting. Further study is needed to determine reasons for FEIAn recurrence.

OIT with a causative food has recently been applied to refractory patients with food allergies.⁵ A few reports have described individuals who developed anaphylaxis during and/or after OIT.^{6,7} These reactions associated with OIT have become a new issue in schools. In this study, we found one student who had anaphylaxis associated with this therapy. Because similar cases may increase in the near future, we should pay more attention to cases of anaphylaxis during physical exercise in students undergoing immunotherapy.

Desensitization and tolerance are different conditions in OIT. Those who had not reached tolerance with OIT are at a high risk of developing anaphylaxis by taking the causative food and exercise. Therefore, we have to recognize that these cases are different from the ordinary cases of FEIAn. With an increase in such cases, misunderstanding and confusion can occur in clinical settings. Thus, we would like to propose a new distinction, i.e., ordinary cases are primary FEIAn and those cases associated with OIT are secondary FEIAn.

The frequency of FEIAn and causative foods has not changed over 14 years, and most junior-high-school nurses at least now

recognize this condition. Preventive measures in schools have significantly improved. Progress in diagnosis and appropriate education in the medical setting are essential to reduce the recurrence of FEIAn. Furthermore, school nurses should be appropriately educated about the condition.

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Conflict of interest

The authors have no conflict of interest to declare.

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