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Adverse events and labeling issues related to suspected sesame allergy reported in an online survey

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ABSTRACT

Background: Allergen avoidance is critical for those with immunoglobulin E–mediated food allergy, but can only be successful with accurate product information. Although the Food and Drug Administration maintains the Center for Food Safety and Nutrition Adverse Event Reporting System to collect adverse event (AE) reports related to foods, there is substantial underreporting, and information regarding product labeling issues is limited.
Objective: The purpose of this study was to describe allergic reactions associated with accidental oral exposure to sesame and the role of product labeling.
Methods: A questionnaire was developed and disseminated to online communities focused on sesame allergy. The questionnaire included questions on clinical characteristics, treatments, outcomes, and labeling issues.
Results: A total of 360 clinical reactions related to sesame were reviewed in 327 individuals. Anaphylaxis occurred in 68.9% of reactions. Hospitalization occurred in 47.8% of events and epinephrine was administered in 36.4% of cases. Events involving a packaged food product occurred in 67.5% of AEs with only 43.8% of these using the term "sesame." An alternative name was noted in 46.0% of products that did not include "sesame" on labeling, most of which was "tahini."
Conclusion: We determined considerable sesame food allergy morbidity, in part owing to inconsistent allergen labeling. Our findings support the development of a more rapid process for the Food and Drug Administration to update the major allergen list and formulation of an improved system for reporting AEs related to foods.

Introduction

Food allergy (FA) is a widespread, potentially life-threatening condition with substantial psychosocial and economic implications.[1-3] It primarily affects the pediatric population with the prevalence of FA in the United States reported being as high as 10% in preschool-aged children.[4,5] The burden of childhood FA is growing, with a recent study reporting an approximately 200% increase in food-induced anaphylaxis–related emergency department visits from 2005 to 2014.[6]

In recent years, increasing evidence has emerged illustrating that sesame allergy is among the more common food allergies.[7] Sesame is a seed native to the Middle East and Africa and is traditionally consumed as tahini, hummus, or halva. In Western countries, sesame seeds are typically used as toppings on bread and crackers and can be used in pharmaceuticals and cosmetics.[8] Globally, sesame is the most common seed to cause immunoglobulin E (IgE)–mediated hypersensitivity and is one of the major causes of IgE-mediated food allergy in Israel.[9,10] Sesame is now the ninth most common childhood FA in the United States with a prevalence of approximately 0.1% to 0.2%.[11]

Studies have found that sesame contains both protein and lipid allergens that can trigger different types of allergic reactions.[12] In a recent study, sesame was associated with reactions of greater severity compared with the other major allergens in oral food challenges.[13] Sesame, along with brazil nut and macadamia nut, had the highest symptom severity scores during oral food challenges in another study, with more involvement of the lower respiratory tract or cardiovascular system.[14] Sesame allergy is thought to mostly be a lifelong condition, with only approximately 20% to 30% of patients outgrowing a sesame sensitivity.[15]

Allergen avoidance is an important part of FA management, but can only be successful if patients and families have access to accurate information on ingredients and possible allergenic contaminants on food labels. The European Union, Canada, Australia, New Zealand, and Israel already require that prepackaged food be

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labeled for sesame.[8,11] The Food Allergen Labeling and Consumer Protection Act of 2004 required peanut, specific types of tree nut, milk, eggs, fish, wheat, soybeans, and shellfish to be declared on food labels, but sesame was not included. The Center for Science in the Public Interest first petitioned the Food and Drug Administration (FDA) to add sesame to the list of major allergens requiring mandatory labeling in November 2014.[16] The agency responded by publishing draft voluntary sesame labeling guidance in November 2020. In April 2021, the United States Congress passed the Food Allergy Safety, Treatment, Education, and Research (FASTER) Act (H.R. 1202/S.578), assuring that sesame allergen labeling will become mandatory in 2023.

The FDA maintains the Center for Food Safety and Nutrition Adverse Event Reporting System (CAERS) to collect adverse event reports related to foods, dietary supplements, and cosmetics.[17,18] However, CAERS' reporting form does not capture key information for food allergies, such as the time between consumption and reaction, other foods consumed, and use of epinephrine. It also includes fields that are not relevant to food, such as product type (over-the-counter, compounded by a pharmacy or outsourcing facility, generic, and biosimilar), strength, and "why was the person using the product?" FDA has received few reports of sesame allergic reaction through CAERS: a search for "sesame" in the publicly available spreadsheet of CAERS reports from 2018, for example, revealed only 1 report listing "anaphylactic reaction" as a symptom.

The objectives of this study were: (1) to describe allergic reactions associated with accidental exposure to sesame in the United States, and (2) to describe the role of allergen labeling in unintentional sesame exposure.

Methods

Protocol and Data Inclusion

The research team developed a questionnaire to collect information on sesame reactions. The survey was based on the CAERS instrument but was tailored to include items that were most relevant to eliciting details regarding suspected FA reactions and food labeling and excluded items (eg, those related to drugs or devices) that were not relevant. The survey was posted online using SurveyMonkey from October 1, 2018 through December 31, 2018. The survey was disseminated by means of social media (Facebook) and e-mail to organizations and online communities focused on food allergies and sesame allergy in particular. The survey allowed respondents to report events that occurred to themselves or another individual. Questions assessing sesame allergic reactions and labeling included basic demographic information and atopic history of the individual who experienced the reaction, type of reaction, when the event took place, symptoms, outcomes, treatment, product details and labeling, and narrative details of the experience. Individual events were not limited to the time frame in which the survey was accessible.

Responses were downloaded from SurveyMonkey, deidentified, and manually screened for inclusion. All responses were reviewed by a board-certified allergist to determine whether allergic reactions met the criteria for anaphylaxis as per the National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network (NIAID/FAAN) criteria.[19] Single responses that listed multiple different events pertaining to allergic reactions to sesame or negative encounters regarding labeling were counted as individual events. Responses recorded at different times from the same internet protocol address (implying the same patient) were also reviewed and counted as individual events when applicable. The primary interest of this study was food-specific sesame exposure causing allergic reactions, and therefore, reactions from cosmetics were excluded from the analyses. Institutional review board approval was not required owing to the use of deidentified information.

Statistical Analyses

Basic demographic information and FA and asthma history were reviewed. Categorical data were analyzed in Microsoft Excel (V14.5.0, Microsoft, Albuquerque, New Mexico) using descriptive statistics. Advanced statistics, which included Fisher's exact test, were performed using GraphPad Version 9.1.0 (Prism Software, San Diego, California). Responses that did not involve allergic reactions to sesame or labeling issues were removed.

Results

Demographics

We reviewed a total of 379 reported events related to sesame encompassing 327 individuals with 360 distinct adverse clinical reactions and 19 events involving a sesame labeling issue without a clinical reaction. A large proportion of respondents (85.6%) were parents or caregivers completing the survey on behalf of their children. Demographic characteristics of the individuals who experienced the adverse reactions are reported in Table 1. As presented in Table 1, 45.6% of individuals were reported as male and 36.1% as female. Children between the ages of 1 and 5 years represented 41.0% of the cohort; 60.0% were White. A history of asthma was reported in 26.3% and the majority had a history of other food allergies (66.7%). Of all respondents, 51.7% reported an allergy to tree nuts and 40.1% to peanuts. A diagnosis of sesame allergy by a physician was noted in 75.2%

Table 1
Demographics and Characteristics of Individuals Who Reported Adverse Clinical Reactions Associated With Sesame Exposure (Overall N = 327)

Sex	N (%)
Male	149 (45.6)
Female	118 (36.1)
N/A	60 (18.3)
Age	
Infant (<1 y)	30 (9.2)
Child age 1-5 y	134 (41.0)
Child age 5-12 y	49 (15.0)
>12 y	45 (13.8)
N/A	69 (21.1)
Race/Ethnicity	
White only	196 (60.0)
Multiracial	20 (6.1)
Asian only	15 (4.6)
Black/African American only	2 (0.6)
American Indian or Alaska Native	1 (0.3)
Hispanic/Latino only	0 (0)
N/A	93 (28.4)
History of asthma?	
Yes	86 (26.3)
No	167 (51.1)
N/A	74 (22.6)
Other food allergies	
Yes	218 (66.7)
Tree nut	169 (51.7)
Peanut	131 (40.1)
Egg	82 (25.1)
Milk/dairy	46 (14.1)
Wheat	22 (6.7)
Fish	16 (4.9)
Shellfish	17 (5.2)
Soy	16 (4.9)
Diagnosed as having sesame allergy by a physician?	
Yes	246 (75.2)
Skin prick test	181 (55.4)
Serum sesame IgE	177 (54.1)
Oral food challenge	8 (2.4)
Elimination diet	12 (3.7)
No	13 (4.0)
N/A	68 (20.8)

Abbreviations: IgE, immunoglobulin E; N/A, not available.

with most having been tested by either skin prick testing (55.4% of all respondents) or serum-specific immunoglobulin testing (54.1%). There were no significant differences found between individuals who had a physician-diagnosed sesame allergy and individuals without a confirmed sesame allergy diagnosis for the following measures of disease severity: events meeting criteria for anaphylaxis (P = .15), epinephrine administration (P = .61), and the need to seek care at an emergency department or hospital (P > .99). There were significant differences between the 2 groups in terms of the history of asthma (P < .001) and history of additional food allergies (P < .001).

Clinical Reactions After Sesame Consumption

Table 2 describes the 360 adverse clinical reactions that were suspected to be related to sesame. The most common reason for reporting an event was the occurrence of an allergic reaction after ingestion (99.4%) as opposed to contact-only exposure with a food product.

Table 2
Characteristics and Severity of Clinical Reactions After Sesame Exposure (Overall N = 360)

Type of exposure	N (%)
Food product was ingested	358 (99.4)
Food product was touched	2 (0.6)
Location of incident	
Home	230 (63.9)
Restaurant	42 (11.7)
Friend's house	19 (5.3)
School	17 (4.7)
Car	8 (2.2)
Work	6 (1.7)
Daycare/after school program/camp	6 (1.7)
Relative's house	5 (1.4)
Hotel	4 (1.1)
Grocery store	4 (1.1)
Playground/park	2 (0.6)
Other	10 (2.8)
N/A	7 (1.9)
Time between exposure and reaction	N (%)
<30 min	260 (72.2)
30 min-1 h	26 (7.2)
>1 h	6 (1.7)
N/A	68 (18.9)
Symptoms	
Skin/cutaneous	327 (90.8)
ENT/respiratory	186 (51.7)
Gastrointestinal	189 (52.5)
Cardiovascular	53 (14.7)
Neurologic	41 (11.4)
Severity of symptoms	
Did reaction meet the criteria for anaphylaxis?	
Yes	248 (68.9)
No	112 (31.1)
Did reaction include cardiovascular ± neurologic system?	
Yes	72 (20)
No	288 (80.0)
Outcome	
Hospitalization or ED visit	172 (47.8)
Observation	17 (4.7)
Doctor's office, urgent care, EMS	12 (3.3)
Death	0 (0)
N/A	159 (44.2)
Treatment	
Epinephrine	131 (36.4)
1 dose epinephrine	62 (17.2)
2 doses epinephrine	23 (6.4)
3 doses epinephrine	4 (1.1)
Did not quantify	42 (11.7)
No epinephrine	224 (62.2)
N/A	5 (1.4)

Abbreviations: EMS, emergency medical service; ENT, ear, nose, throat; ED, emergency department; N/A, not available.

Most of the events occurred at home (63.9%), approximately 11.7% of events occurred at a restaurant, 5.3% at a friend's house, and 4.7% of events occurred at school.

The onset of symptoms was less than 30 minutes after sesame consumption in 72.2% of reported reactions. Individuals reported reactions with involvement of the skin (90.8%), respiratory system including involvement of ears, nose, and throat (51.7%), gastrointestinal system (52.5%), cardiovascular system (14.7%), and neurologic system (11.4%). A large proportion of reactions met the NIAID/FAAN criteria for anaphylaxis (68.9%). Approximately 48% of reactions required hospitalization or an emergency department visit. Overall, 36.4% of total reactions were treated with epinephrine, however, epinephrine was used in only 48.8% of reactions meeting the criteria for anaphylaxis.

Product Characteristics and Labeling

As listed in Table 3, product-specific information for a total of 379 adverse reactions and labeling errors were reviewed. Questions regarding which the product was purchased and details of sesame labeling or lack thereof on the product were frequently left unanswered. Reported events owing to a product that was purchased at a grocery store represented 37.7% of the cohort, followed by approximately 9.0% purchased at a restaurant. Other locations where products containing sesame were purchased include bakeries, delis, hotels, and an online food subscription service. Approximately two-thirds of events (67.5%) occurred with a product that was sold in a package with a label, whereas 10.0% were associated with a product without a label. A total of 112 products (43.8% of the total number of packaged and labeled products) included the term "sesame" on labeling, most of which (n = 103) declared "sesame" in the ingredients list. An alternate name to "sesame" used on packaged and labeled products was reported in 46.0% of products; "tahini" was used most frequently (80.3% of products that used an alternate name). A few products (9.1%) were simply labeled as "spices or natural flavor." Of the 144 cases in which sesame was suspected to be the cause of a reaction but not declared on the label, 32 (22.2%) reported no food allergies other than sesame, and 78 (54.2%) events met the criteria for anaphylaxis.

Table 3
Characteristics of Products Leading to Adverse Reactions or Labeling Errors (Overall N = 379)

Where was the product purchased?	N (%)
Grocery store	143 (37.7)
Restaurant	34 (9.0)
Other (Deli, bakery, hotel, online)	7 (1.8)
N/A	195 (51.4)
Was the product sold in a labeled package?	
Product was sold in a package with a label	256 (67.5)
Product was sold without a label	38 (10.0)
N/A	85 (22.4)
Was "sesame" included on labeled package?	N = 256
Yes	112 (43.8)
In the ingredients list	103 (40.2)
;In a "may contain statement"	3 (11.7)
In a "contains" statement	0 (0)
Elsewhere on the label	6 (2.3)
No	144 (56.2)
Was an alternate name used on the product?	N = 144
Yes	66 (46.0)
No	62 (43.0)
N/A	16 (11.1)
Alternate name used on the product	
Tahini	53 (80.3)
Spices and/or natural flavors	6 (9.1)
N/A	7 (10.6)

Abbreviation: N/A, not available.

Discussion

This study presented a high rate of potential accidental sesame reactions in individuals with sesame allergy, inadequate and inconsistent allergen labeling for sesame, and poor FA reporting within established reporting systems in the United States. More than half of products did not declare sesame on the label (56.2%); 48% of events resulted in an emergency department visit or hospitalization, and approximately 69% of all reactions met the NIAID/FAAN criteria for anaphylaxis.

Our results are consistent with previous findings that the proportion of anaphylactic reactions owing to accidental sesame ingestion among those with a sesame allergy is high.[16] The discrepancy between the proportion of anaphylactic events and epinephrine administration may reflect an underrecognition of anaphylaxis, underutilization of epinephrine in the setting of anaphylaxis, or underappreciation of sesame as a cause of anaphylaxis.

We suspect that inconsistent labeling of sesame products likely contributed to accidental reactions, such as using tahini, a term that some may not associate with sesame. For example, 1 parent reported, "Sabra hummus was her first reaction. I did not know until later that hummus used tahini and tahini was crushed sesame." A few events were owing to products declared as containing "spices" or "natural flavors" and required the consumer to call the company or manufacturer to clarify the ingredients. One of the reported events occurred in a child with known sesame allergy who had meatloaf that was made with breadcrumbs. The parents later learned from the manufacturer that the "spices" labeled on the breadcrumbs contained sesame. This information further emphasizes the importance of clear and specific product labeling for sesame.

In one case, a parent reported that their child developed nausea, vomiting, and abdominal pain after eating pita bread that did not list sesame as an ingredient. The parent saved the pita in the freezer and gave the pita to the child again a few months later with recurrence of the same gastrointestinal symptoms. The parent sent the pita to a laboratory for testing, and the laboratory confirmed that the pita contained sesame. These examples illustrate the inherent danger of poor labeling in those with an IgE-mediated FA to sesame.

The primary limitation of this study is that the data are self-reported and incidences cannot be calculated. Individuals who experienced a more serious reaction or event may have been more likely to respond to the survey, which would skew the results toward a higher proportion of severe reactions to sesame than in the general population with sesame allergy. Recruiting individuals from online allergy communities who may already have a heightened awareness of FA could have produced a similar effect, resulting in data that may not be generalizable. Item nonresponse was also an issue, particularly for questions related to patient demographics, location of purchase, and product labeling. In addition, the short time in which the survey was made available may have limited the number of responses.

Another major limitation is the inability to verify that all the reported adverse events were truly due to sesame and not caused by another food allergen, allergic disease, or nonallergic event. As seen in the results, there were no significant differences in allergic reaction severity between individuals with a physician-confirmed sesame allergy and individuals without a sesame allergy diagnosis. However, there were significant differences between the 2 groups in terms of a history of asthma and history of other food allergies, which may indicate that those with a physician-confirmed sesame allergy are also more likely to have an additional evaluation of atopic comorbidities. The data suggest that there is substantial room for allergists to improve their education of patients regarding sesame avoidance and how to read food labels. Finally, it is conceivable that, since the time of data collection in 2018, labeling in compliance with the FASTER Act by certain companies may already be reducing the risk of accidental sesame exposures.

In conclusion, clear and specific product labeling for sesame is crucial for the prevention of adverse reactions, especially anaphylaxis, in food-allergic consumers. Our data support the addition of sesame as a major food allergen as established by the FASTER Act. Given that it took nearly a decade to secure mandatory sesame labeling through legislation, we strongly recommend the implementation of a new, more rapid process that would allow the FDA to make future updates to the list of major allergens more easily on the basis of prevalence and severity data pertaining to FA. We suggest that there remains significant potential for improvement in systemic and standardized monitoring of adverse events related to food exposure that would be useful both in broadening our understanding of accidental food reactions and the potential impact of inadequate labeling.

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