Clinical Communications

Initial and accidental reactions are managed inadequately in children with sesame allergy

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Clinical Implications

- Sixty-two percent of children with sesame allergy present with anaphylaxis, and among those with a known allergy, the annual rate of accidental exposure is 15.9%. Most initial reactions and accidental exposures are managed inadequately, emphasizing the need for improved education.

TO THE EDITOR:

In population-based studies, the prevalence of sesame allergy in children is estimated at 0.1% (95% confidence interval [CI], 0.0, 0.3) in Canada[1] and the United States,[2] 0.2% (95% CI, 0.1, 0.3) in Israel,[3] and up to 0.8% (95% CI, 0.5, 1.1) in Australia.[4] Differences likely reflect varying study designs, diagnostic criteria, and dietary practices. Because of its rarity compared with peanut allergy, which has a prevalence of 2% in children,[1] little is known about how sesame allergy manifests in North American children. Here, we describe the initial presentation and annual incidence rate, severity, management, and location of accidental exposures (AEs) and identify factors associated with AE and anaphylaxis at the initial reaction.

Children with physician-confirmed sesame allergy were recruited from allergy clinics at the Montreal Children's Hospital (MCH) between February 2008 and July 2013 and from Canadian allergy advocacy organizations between February 2009 and March 2012. Parents completed a questionnaire at study entry regarding their child's initial reaction to sesame and AEs to sesame over the preceding year. Reaction details included the food ingested and the signs, symptoms, treatment, and location. Parents also reported on demographics, the allergic child's and family history of atopy (ie, other food allergy, eczema, or asthma), and prescription of the epinephrine autoinjector.

The study was approved by the McGill University Health Centre Research Ethics Board.

Children were allergic to sesame if they had:

- a convincing history[5,6] of an allergic reaction and a positive skin prick test (SPT) $\geq$ 3 mm to sesame (for the majority, with commercial extract from ALK-Abello Pharmaceuticals, Mississauga, Ontario, Canada) or
- a positive oral challenge to sesame (with either sesame seeds or tahini).

A convincing clinical history referred to at least 2 mild signs and/or symptoms or 1 moderate or severe sign and/or symptom that was likely IgE mediated and occurred within 120 minutes after sesame ingestion or contact. Reactions were considered mild if they included pruritus, urticaria, flushing, or rhinoconjunctivitis; moderate if angioedema, throat tightness, gastrointestinal complaints, or breathing difficulties (other than wheeze); and severe if wheeze, cyanosis, or circulatory collapse.[5,6]

The age of diagnosis of sesame allergy was based on the earliest age at the time of the first reaction, first positive SPT, or positive challenge to sesame.

Descriptive statistics were compiled for all variables. The annual incidence rate of AE was expressed as the number of events divided by the sum of the patient-years at risk.

Univariate and multivariate logistic regression analyses were used to examine potential predictors of the odds of (1) experiencing an AE and (2) experiencing anaphylaxis (based on the consensus definition[7]) at the initial reaction. Potential predictors for regression 1 included sex, ethnicity, age at recruitment, disease duration at recruitment, observation interval, source of recruitment, personal atopic conditions, severity of the initial reaction to sesame, and parental demographic factors. Predictors for regression 2 included sex, ethnicity, age at the initial reaction, source of recruitment, personal atopic conditions, size of initial positive SPT, form of sesame ingested and interval between sesame ingestion and symptom onset at the initial reaction, location of the initial reaction, parental demographic features, and family history of atopy. For the most informative multivariate models, only the remaining statistically significant predictors at the 95% CI were included, after eliminating all other potential predictors individually, starting with the least likely to be associated with the outcome.

Of 204 patients surveyed, 115 responded with 88 (76.5%) recruited from the MCH (Table I). Nonrespondents (n = 89) were older at diagnosis than respondents (3.9 years, 95% CI, 3.2, 4.6 vs 2.4 years, 95% CI, 2.1, 2.8) and had shorter disease duration at recruitment (3.3 years vs 4.6 years, yielding a difference of 1.3 years, 95% CI, 0.1, 2.4). However, nonrespondents were similar to respondents regarding sex (56.2% males, 95% CI, 45.3, 66.7 vs 58.3%, 95% CI, 48.7, 67.4) and age at recruitment (7.1 years, 95% CI, 6.1, 8.1 vs 7.0 years, 95% CI, 6.1, 7.9).

Respondents were predominantly white (87.8%) (Table I). The patients were highly atopic, with 82.6% reporting another food allergy (47.0% of the 115 reporting peanut allergy of which 59.3% [95% CI, 45.0, 72.4] had been confirmed with history and positive SPT and/or challenge), 63.5% reporting eczema, and 50.4% reporting asthma.

Four participants were included based on a positive food challenge and 111 based on a convincing clinical history and positive SPT. The average size of the initial positive SPT was 8.4 mm (range, 3-20 mm).

The initial reaction was mild in 20.9% of patients, moderate in 70.4%, and severe in 8.7%. Of the 115 patients, 71 (61.7%) presented with anaphylaxis. Among the 24 mild reactions, 8 were not treated, 15 were treated only at home, and only 1 sought medical attention; none received epinephrine. Among the 81

TABLE I. Demographic and clinical characteristics of participants

	N = 115
Male (%)	58.3
Ethnicity (% white)	87.8
Age at diagnosis,* (y), mean (SD)	2.4 (1.9)
Age at the initial reaction (y), mean (SD)	2.6 (2.2)
Age at recruitment (y), mean (SD)	7.0 (4.7)
Disease duration at recruitment (y), mean (SD)	4.6 (4.3)
Recruited through Montreal Children's Hospital (%)	76.5
Personal history of other food allergy (%)	82.6
Personal history of eczema (%)	63.5
Personal history of asthma (%)	50.4
Skin prick test,† wheal diameter, mean, mm (SD)	8.4 (3.7)
Initial reaction moderate/severe‡ (%)	79.1
Initial reaction severe (%)	8.7
Form of sesame ingested at the initial reaction, paste (%)	60.0
Interval between ingestion and symptoms at the initial reaction, less than 5 min (%)	53.0
Location of the initial reaction, home (%)	70.3
Single parent household (%)	6.1
Age of parents (y), mean (SD)	40.6 (6.3)
Mother's education and work status (%)	
Post-secondary education	94.7
Completed university	71.1
Currently employed	68.7
Father's education and work status (%)	
Post-secondary education	86.4
Completed university	64.5
Currently employed	87.8
Family history of atopy (%)	77.4

SD, Standard deviation.
*The age of diagnosis of sesame allergy was the earliest of the age of the first reaction or confirmatory testing.
†Refers to initial positive skin prick test; wheal diameter not provided for 4 patients with a positive skin prick test.
‡Mild signs and/or symptoms: pruritus, urticaria, flushing, rhinoconjunctivitis; moderate: angioedema, throat tightness, gastrointestinal complaints, breathing difficulties other than wheeze; severe: wheeze, cyanosis, circulatory collapse.[5,6]

moderate reactions, 19 were not treated, 42 were treated only at home, and 20 sought medical attention; 6 of those treated at home used an epinephrine autoinjector and 7 seeking medical attention received epinephrine at a health care facility. Among the 10 severe reactions, 4 were treated only at home and 6 sought medical attention; 3 of those treated at home used an autoinjector and 2 seeking medical attention received epinephrine at a health care facility.

Sixty percent (69 children) reacted to sesame paste (in 49 it was hummus alone, in 5 it was a hummus/tahini mixture, and in 15 it was tahini alone), 30.4% to sesame seeds, 5.2% to candy, and in 4.3% it was unspecified. Fifty-three percent reacted within <5 minutes of ingesting sesame and 40.9% between 5 and 30 minutes of ingestion. Seventy percent of initial reactions occurred at home.

Sixteen AEs occurred in 115 children over 100.4 patient-years, yielding an annual incidence rate of 15.9% (95% CI, 9.1, 25.9). Five of the AEs were mild (2 were not treated, 2 were treated at home, and 1 sought medical attention; none received epinephrine), 9 moderate (2 were not treated, 6 were treated at home, and 1 sought medical attention and received epinephrine), and 2 severe (1 was not treated and 1 was treated at home with an autoinjector). Among the 16 AEs, 3 of the corresponding initial reactions to sesame were mild, 11 were moderate, and 2 were severe. Two AEs were more severe than the initial reaction, 4 were less severe, and 10 were of comparable severity.

Fifty percent of AEs occurred at home, and there were 2 AEs in schools, 2 AEs in restaurants, and 1 AE each in a sports venue, a friend's house, a vehicle, and an unknown location.

Of the 110 patients who provided details on the availability of the autoinjector, 68 (61.8%) indicated that it had first been prescribed for another food allergy, and 93.6% of respondents owned more than 1. Of the 68 patients who indicated that the autoinjector had first been prescribed for another food allergy, 43 already possessed it before their initial reaction to sesame and another 6 already possessed it for a non-food allergy. Among the 43 patients, only 4 used the autoinjector to treat their initial reaction to sesame, which was moderate in 3 cases, and severe in 1 case. Among the additional 6 patients, 2 used the autoinjector to treat their initial reaction to sesame, which was moderate in both cases. Three had access to a sibling's autoinjector and used it to treat their initial reaction to sesame, which was moderate in 1 case and severe in 2 cases. For those 16 patients who experienced an AE, 14 had their autoinjector prescribed before the AE (unknown for the other 2), but only 1 of the 14 used it to treat their AE. Among the 49 patients who possessed the autoinjector before their initial reaction to sesame either for a food allergy (43) or for a non-food allergy (6), 40 (81.6%) were educated in its use.

Children with eczema (odds ratio [OR]: 0.29; 95% CI, 0.10, 0.89) were less likely to experience an AE, whereas older children (OR: 1.12; 95% CI, 1.00, 1.25) were more likely to have an AE (Table II).

Older children (OR: 1.29; 95% CI, 1.03, 1.61) and those with a family history of atopy (OR: 2.69; 95% CI 1.06, 6.85) were more likely to experience anaphylaxis at the initial reaction (Table II).

This is the largest North American study of children with sesame allergy. Because of the relative rarity of sesame allergy, the sample is much smaller than our studies involving children with peanut allergy and our estimates for the annual rate of AE are less precise. Nonetheless, our study suggests that Canadian children with sesame allergy experience an annual rate of AE (15.9%, 95% CI, 9.1, 25.9) that is reasonably comparable to the AE rate for children with peanut allergy (12.4%, 95% CI, 11.4, 13.4).[8] Also similar to peanut allergy, the majority of children who experienced moderate to severe initial reactions and AEs did not seek medical attention and even in those who did, epinephrine was underutilized.[9] The underusage of the autoinjector is particularly concerning as 49 children already possessed an autoinjector at the time of their initial reaction to sesame and the majority were educated on its use, yet only 6 used it. Further, at least 14 of the 16 children experiencing an AE possessed an autoinjector and only 1 used it.

In this study, children with eczema and younger children were less likely to experience an AE. This may be because these children are perceived to be at higher risk and caregivers may exercise more caution. Older children were more likely to experience an AE because they exhibit more risky behaviours regarding their diet and eating behaviours and are more often unobserved.

TABLE II. Univariate and multivariate predictors of (1) accidental exposures or (2) anaphylaxis at the initial reaction

	Predictors of accidental exposures		Predictors of anaphylaxis at the initial reaction	
	Univariate OR (95% CI)	Most informative multivariate OR (95% CI)	Univariate OR (95% CI)	Most informative multivariate OR (95% CI)
Male	1.23 (0.41, 3.64)		1.28 (0.60, 2.74)	
White	2.27 (0.28, 18.64)		1.24 (0.40, 3.86)	
Age at the initial reaction (as a continuous variable)	N/A*		1.26 (1.01, 1.56)	1.29 (1.03, 1.61)
Age at recruitment (as a continuous variable)	1.12 (1.01, 1.25)	1.12 (1.002, 1.25)	N/A	
Disease duration at recruitment	1.09 (0.97, 1.22)		N/A	
Observation interval (in mo, as it was <12 mo for those who entered the study within <12 mo of disease duration)	1.09 (0.88, 1.34)		N/A	
Recruitment from allergy advocacy associations (vs Montreal Children's Hospital)	0.72 (0.19, 2.75)		2.07 (0.79, 5.41)	
Personal history of other food allergies	0.90 (0.23, 3.5)		1.09 (0.41, 2.93)	
Personal history of eczema	0.29 (0.10, 0.86)	0.29 (0.10, 0.89)	1.16 (0.53, 2.52)	
Personal history of asthma	0.73 (0.25, 2.12)		0.89 (0.42, 1.88)	
Size of initial positive SPT	N/A		1.02 (0.92, 1.14)	
Initial reaction moderate/severe	1.17 (0.30, 4.48)		N/A	
Initial reaction severe	1.63 (0.31, 8.45)		N/A	
Seeds ingested at the initial reaction (vs other form)	N/A		0.81 (0.36, 1.82)	
Interval between contact and symptoms <5 min at the initial reaction (vs ≥5 min)	N/A		1.41 (0.66, 3.01)	
Initial reaction at home (vs elsewhere)	N/A		0.46 (0.18, 1.15)	
Single parent household	2.69 (0.47, 15.20)		0.82 (0.17, 3.83)	
Age of parents	1.08 (1.00, 1.17)		1.06 (1.00, 1.14)	
Mother completed university	0.46 (0.16, 1.37)		0.77 (0.33, 1.79)	
Mother currently employed	0.53 (0.18, 1.57)		1.04 (0.46, 2.34)	
Father completed university	1.25 (0.40, 3.89)		0.72 (0.32, 1.66)	
Father currently employed	0.54 (0.13, 2.20)		2.41 (0.77, 7.48)	
Family history of atopy	N/A		2.29 (0.94, 5.57)	2.69 (1.06, 6.85)

CI, Confidence interval; *OR*, odds ratio; *SPT*, skin prick test.
*N/A refers to not applicable and indicates that the variable was not included in the model as a potential predictor.

Similarly, older children were more likely to present with anaphylaxis at the initial reaction because they are more likely to try new foods, potentially in large quantities, and often unobserved. Hence, an allergic reaction may be treated less promptly, and is therefore more likely to progress to anaphylaxis. It is also possible that older children chew the sesame seeds more, resulting in more absorption and exposure to allergenic proteins in sesame and an increased likelihood of anaphylaxis at the initial reaction. Those with a family history of atopy were also more likely to present with anaphylaxis, potentially because parents familiar with atopy may be more likely to recognize and report symptoms of anaphylaxis in their child than parents unfamiliar with allergy. Because of the small sample size, we may not have been able to detect an association between other predictors and the risk of AE or presenting as anaphylaxis at the initial reaction. The study may have limited generalizability as the large majority of children were white and parents were highly educated.

Despite increasing efforts to enhance understanding of food allergy, AEs in children with known sesame allergy continue to occur, mainly in the child's home, and many moderate and/or severe AEs are managed inadequately. Therefore, current educational efforts addressing the need for strict allergen avoidance and prompt and correct management of anaphylaxis need to be re-examined and improved.

Author contributions

L.S., M.B-S., R.A., M-N.P., Y.A., E.C., S.C., G.S., YS.-P., and A.C. were responsible for conception and design. L.S., MB.-S., R.A., M-N.P., Y.A., K.R.K., E.C., L.H., and A.C. were responsible for acquisition of data. L.S., MB.-S., R.A., M-N.P., Y.A., E.C., S.C., G.S., Y.S-P., and A.C. were responsible for analysis and interpretation of data. LS, AC drafted the article. L.S., M.B-S., R.A., M-N.P., Y.A., K.R.K., E.C., S.C., Y.S-P., and A.C. were responsible for revision of the article critically for important intellectual content: All authors have approved the final version of the article.

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