



Sesame-induced anaphylaxis in pediatric patients from the cross-Canada anaphylaxis registry



Carly Sillcox, BSc^{*}; Sofianne Gabrielli, MSc^{*}; Ann E. Clarke, MD, MSc[†]; Judy Morris, MD, MSc[‡]; Jocelyn Gravel, MD, MSc[§]; Rodrick Lim, MD^{||}; Edmond S. Chan, MD[¶]; Ran D. Goldman, MD[#]; Andrew O'Keefe, MD^{**}; Jennifer Gerdts, BComm^{††}; Derek K. Chu, MD, PhD^{‡‡,§§}; Julia Upton, MD, MPH^{||||}; Elana Hochstadter, MD^{¶¶}; Jocelyn Moisan, MD, MSc^{##}; Adam Bretholz, MD^{***}; Christine McCusker, MD, MSc^{*}; Xun Zhang, PhD^{†††}; Jennifer L.P. Protudjer, PhD^{†††,§§§,|||||,¶¶¶,###}; Elissa M. Abrams, MD, MPH^{****}; Elinor Simons, MD, PhD^{****}; Moshe Ben-Shoshan, MD, MSc^{*}

^{*} Division of Allergy and Clinical Immunology, Department of Pediatrics, Montreal Children's Hospital, McGill University Health Centre, Montreal, Quebec, Canada

[†] Division of Rheumatology, Department of Medicine, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

[‡] Department of Emergency Medicine, Sacré-Coeur Hôpital, Montreal, Quebec, Canada

[§] Department of Pediatric Emergency Medicine, Centre Hospitalier Universitaire Sainte-Justine, Université de Montréal, Montreal, Quebec, Canada

^{||} Division of Pediatric Emergency Medicine, Department of Pediatrics, Children's Hospital at London Health Science Centre, London, Ontario, Canada

[¶] Division of Allergy and Immunology, Department of Pediatrics, BC Children's Hospital, The University of British Columbia, Vancouver, British Columbia, Canada

[#] Division of Clinical Pharmacology and Emergency Medicine, Department of Pediatrics, BC Children's Hospital, The University of British Columbia, Vancouver, British Columbia, Canada

^{**} Department of Pediatrics, Faculty of Medicine, Memorial University, St. John's, Newfoundland and Labrador, Canada

^{††} Food Allergy Canada, Toronto, Ontario, Canada

^{‡‡} Division of Clinical Immunology and Allergy, Department of Medicine, McMaster University, Hamilton, Ontario, Canada

^{§§} Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON, Canada

^{||||} Division of Immunology and Allergy, Department of Pediatrics, The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada

^{¶¶} Department of Pediatric Emergency Medicine, The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada

^{##} Emergency Medical Services of Outaouais, Outaouais, Quebec, Canada

^{***} Division of Pediatric Emergency Medicine, Department of Pediatrics, Montreal Children's Hospital, Montreal, Quebec, Canada

^{†††} Centre for Outcomes Research and Evaluation, The Research Institute of McGill University Health Centre, Montreal, Quebec, Canada

^{§§§} Department of Pediatrics and Child Health, University of Manitoba, Winnipeg, Manitoba, Canada

^{|||||} Food and Human Nutritional Sciences, University of Manitoba, Winnipeg, Manitoba, Canada

^{¶¶¶} Children's Hospital Research Institute of Manitoba, Winnipeg, Manitoba, Canada

^{###} George and Fay Yee Centre for Healthcare Innovation, Winnipeg, Manitoba, Canada

^{****} Centre for Allergy Research, Karolinska Institute, Stockholm, Sweden

^{****} Section of Allergy and Clinical Immunology, Department of Pediatrics and Child Health, Children's Hospital Research Institute of Manitoba, Winnipeg, Manitoba, Canada

ARTICLE INFO

Article history:

Received for publication April 5, 2022.

Received in revised form June 2, 2022.

Accepted for publication June 2, 2022.

ABSTRACT

Background: Sesame can cause severe allergic reactions and is a priority allergen in Canada.

Objective: To assess clinical characteristics and management of pediatric sesame-induced anaphylaxis and identify factors associated with epinephrine treatment.

Methods: Between 2011 and 2021, children with sesame-induced anaphylaxis presenting to 7 emergency departments (ED) in 4 Canadian provinces and 1 regional emergency medical service were enrolled in the Cross-Canada Anaphylaxis Registry. Standardized recruitment forms provided data on symptoms, severity, triggers,

Reprints: Carly Sillcox, BSc, Division of Pediatric Allergy and Clinical Immunology, McGill University Health Centre, 1001 Blvd. Decarie, Montreal, Quebec, Canada, H4A 3J1. Tel: 289-894-1600. E-mail: carly.sillcox@mail.mcgill.ca.

Disclosures: Dr Upton reports receiving research support/grants from Novartis, Regeneron, ALK, DBV, and CIHR; and fees from AstraZeneca, Pfizer, ALK Abello, Bausch Health, Kaleo, and Food Allergy Canada, all outside the submitted work. Ms Gerdts is an employee of Food Allergy Canada, which receives some funding support from Pfizer, Kaleo, and Bausch, all of which are suppliers of epinephrine autoinjectors. Dr Chan

reports receiving research support from DBV Technologies; has been a member of advisory boards for Pfizer, Padiapharm, Leo Pharma, Kaleo, DBV, AllerGenis, Sanofi Genzyme, Bausch Health, and Avir Pharma; is on the executive committee of the Canadian Society of Allergy and Clinical Immunology; is on the executive committee of the Canadian Paediatric Society Allergy Section; and is a member of the healthcare advisory board for Food Allergy Canada. The remaining authors have no conflicts of interest to report.

Funding: This study was funded by AllerGen NCE, Inc.

and management. Multivariate logistic regression evaluated associations with epinephrine treatment pre-ED and multiple epinephrine dosages.

Results: Of all food-induced anaphylactic reactions ($n = 3279$ children), sesame accounted for 4.0% ($n = 130$ children), of which 61.5% were boys, and the average (SD) age was 5.0 (4.9) years. Hummus containing sesame paste triggered 58.8% of reactions. In the pre-ED setting, 32.3% received epinephrine, and it was more likely to be used in boys (adjusted odds ratio [aOR], 1.27; 95% confidence interval [CI], 1.08–1.50) and those with a known food allergy (aOR, 1.36; 95% CI, 1.11–1.68)]. In the ED, 47.7% of cases received epinephrine, with older children more likely to receive multiple epinephrine doses (aOR, 1.00; 95% CI, 1.00–1.02).

Conclusion: In Canada, hummus is the major trigger of sesame-induced anaphylaxis. Knowledge translation focused on prompt epinephrine use and product-labeling policies are required to limit sesame reactions in communities.

© 2022 American College of Allergy, Asthma & Immunology. All rights reserved.

Introduction

Sesame allergy affects 0.2% of children in North America and is a major cause of anaphylaxis in the Middle East.^{1,2} Sesame (*Sesamum indicum* L.) is found in various food items and dishes in the form of ground sesame, sesame seeds, sesame oil, or sesame paste (eg, tahini).³ Common items containing this priority food allergen include hummus (chickpea spread containing sesame paste), bagels, bread, crackers, chips, and baked goods. Notably, sesame seeds contain numerous food allergen protein groups associated with sesame sensitization and immunoglobulin E–mediated allergic reactions.³ Such sesame seed allergens include proteins from different protein groups,³ of which the seed storage proteins are associated with severe allergic reactions.

The rise in sesame allergy is largely attributed to food globalization, given that sesame is often found in Middle Eastern and Asian dishes.⁴ However, there are little data on the clinical presentation and management of sesame-induced anaphylaxis in North America. To address this knowledge gap, we assessed the clinical characteristics and management of children with sesame-induced anaphylaxis presenting to Canadian emergency departments (ED) as part of the Cross-Canada Anaphylaxis Registry (C-CARE). We also identify factors associated with epinephrine treatment before the ED and factors associated with multiple doses of epinephrine (2 or more) in the ED.

Methods

Study Design

This cross-sectional study included nationwide pediatric sesame-induced anaphylaxis data collected through C-CARE from April 27, 2011 to January 31, 2021. Pediatric patients with food allergy were enrolled in 7 Canadian EDs in 4 provinces (British Columbia, Ontario, Quebec, and Newfoundland and Labrador) and 1 emergency medical services (EMS) in Quebec's Outaouais region. Patient data were obtained prospectively and retrospectively.⁵ Prospective data were collected during the ED or EMS patient visit. Physicians identified anaphylaxis in children, and trained research members acquired consent from the patients and their families. Standardized recruitment forms were completed on the symptoms, severity, triggers, and anaphylaxis management. Retrospective data were collected for missed cases after ED and EMS visits through a structured chart review on the basis of the International Classification of Diseases 10th Edition codes related to anaphylaxis.⁶ Cases were excluded if they did not align with the definition of anaphylaxis: involvement of at least 2 organ systems or hypotension in response to an allergen, as reviewed independently by 2 members of the research team.^{5,7}

Setting

In Quebec, 4 EDs were involved in the C-CARE: the Montreal Children's Hospital, the Montreal General Hospital, Hôpital Sainte-Justine, and Hôpital du Sacré-Coeur de Montreal. Children managed

by the Quebec's Outaouais region EMS were also recruited for the study. In addition, data from children presenting with anaphylaxis to the London Health Sciences Centre in Ontario, the British Columbia Children's Hospital in British Columbia, and the Janeway Children's Health and Rehabilitation Centre in Newfoundland and Labrador were included in the C-CARE data set.

Participants

Children younger than 18 years of age with sesame-induced anaphylaxis presenting to any C-CARE recruiting EDs or EMS were eligible to participate in the study.

Outcomes and Independent Variables

Outcomes of interest included anaphylaxis severity, epinephrine treatment pre-ED, and the use of multiple epinephrine dosages in the ED. In the pre-ED setting, epinephrine administration was analyzed for associations with age, sex, reaction severity, reaction location, and known food allergy. Independent variables included patient characteristics, sesame triggers, and pre-ED treatments. In the ED, multiple dosages of epinephrine were analyzed for associations with age, sex, and pre-ED treatment with antihistamines and epinephrine. The severity of anaphylaxis was classified as mild, moderate, or severe using a modified grading system.⁸ Mild anaphylaxis included nasal congestion and sneezing, rhinorrhea, throat tightness, mild wheezing, generalized pruritis, flushing, urticaria, angioedema, mild abdominal pain, nausea and vomiting, tachycardia, and anxiety.⁹ Moderate anaphylaxis included harsh cough, moderate wheezing, dysphagia, shortness of breath, crampy abdominal pain, repeated vomiting, diarrhea, and light-headedness.⁹ Severe anaphylaxis included cyanosis, respiratory arrest, hypotension, circulatory collapse, dysrhythmia, bowel incontinence, cardiac arrest or serious bradycardia, confusion, and unconsciousness.⁹

Statistical Analysis

Analyses were completed using R version 4.0.3. (R Core Team [2020]; R: A language and environment for statistical computing; R Foundation for Statistical Computing, Vienna, Austria). Clinical characteristics and demographics were reported as means (SD) for continuous data and as percentages for categorical data. Each variable was dichotomized for statistical purposes, except for age. Factors associated with epinephrine treatment pre-ED and multiple epinephrine dosages in the ED were evaluated using multivariate logistic regression. The significance level was set at .05.

Ethics Approval

All participating hospitals' ethics committees approved the study. Informed consent was obtained for all the participants recruited prospectively.

Results

Demographics and Clinical Characteristics

Over a 10-year study period (April 2011 to January 2021), 3739 food-triggered cases were logged as part of the C-CARE initiative, of which 3279 (88.0%) were pediatric cases. Among the pediatric food-induced anaphylaxis reactions, sesame accounted for 4.0% ($n = 130/3279$) of all cases. The 130 pediatric patients were recruited predominantly from Quebec ($n = 109/119$; 91.6%). The mean age was 5.0 years (SD 4.9 years), and most ($n = 80/130$; 61.5%) were boys. Participating children also had various other allergic conditions, including eczema ($n = 31/130$; 23.8%) and other food allergies ($n = 88/130$; 67.7%), of which peanuts ($n = 35/130$; 26.9%) and nuts ($n = 20/130$; 15.4%) were the most common. Only 37.7% ($n = 49/130$) had a known sesame allergy, and thus 62.3% ($n = 81/130$) had sesame-induced anaphylaxis as the presenting symptom of their sesame allergy. Interestingly, no asthma comorbidity was reported (Table 1).

Most reactions were classified as moderate ($n = 79/130$; 60.8%), whereas 44 cases (33.8%) were considered mild and 7 cases (5.4%) severe. Common symptoms included angioedema ($n = 86/130$; 66.2%), urticaria ($n = 83/130$; 63.9%), pruritus ($n = 59/130$; 45.4%), gastrointestinal symptoms ($n = 48/130$; 36.9%), and breathing difficulties ($n = 35/130$; 26.9%). The most common sesame trigger was hummus (spread containing sesame paste–tahini), causing anaphylaxis in

Table 1
Demographics and Clinical Characteristics of Pediatric Patients With Sesame-Induced Anaphylaxis Presenting to EDs

Variable (N = 130)	Pediatric patients (n, %)
Province: (N = 119)	
Quebec	109 (91.6%)
Ontario	9 (7.6%)
Newfoundland and Labrador	1 (0.8%)
British Columbia	0 (0.0%)
Age at reaction (mean, SD)	5.0 (4.9)
Sex - male	80 (61.5%)
Sex - female	50 (38.5%)
Other condition:	
Known food allergy	88 (67.7%)
Known eczema	31 (23.8%)
Known asthma	0 (0.0%)
Specific known food allergy:	49 (37.7%)
Sesame	35 (26.9%)
Peanut	20 (15.4%)
Nut ^a	15 (11.5%)
Tree nut	16 (12.3%)
Egg	14 (10.8%)
Milk	10 (7.7%)
Fish	3 (2.3%)
Shellfish	
Anaphylaxis severity:	
Mild	44 (33.8%)
Moderate	79 (60.8%)
Severe	7 (5.4%)
Symptoms:	
Angioedema	86 (66.2%)
Urticaria	83 (63.9%)
Pruritus	59 (45.4%)
Gastrointestinal	48 (36.9%)
Breathing difficulties	35 (26.9%)
Flushing	30 (23.1%)
Throat tightness	28 (21.5%)
Sesame trigger: (N = 114)	
Hummus (tahini)	67 (58.8%)
Bagel sesame grains	5 (4.4%)
Bread	4 (3.5%)
Cookie	4 (3.5%)
Oil	3 (2.6%)
Crackers	2 (1.8%)

(continued)

58.8% of cases ($n = 67/114$), followed by bagel sesame grains causing 4.4% of cases ($n = 5/114$), and bread and cookies, each causing 3.5% of cases ($n = 4/114$). Almost half ($n = 58/130$; 48.3%) of the sesame reactions occurred within 5 minutes, whereas 46.7% ($n = 56/130$) occurred between 5 minutes and 2 hours after exposure (Table 1). Note that 3.3% of reactions ($n = 4/130$) occurred between 2 hours and 8 hours and may be related to late recognition, recall bias or rare cases of delayed anaphylaxis.¹⁰

Pre-Emergency Department and Emergency Department Management

In the pre-ED setting, 32.3% ($n = 42/130$) of patients received epinephrine, 50.8% ($n = 66/130$) received antihistamines, 4.6% ($n = 6/130$) received inhaled β agonists, 0.1% ($n = 1/130$) received corticosteroids, and 30.0% ($n = 39/130$) received no treatment. In the ED, 47.7% ($n = 62/130$) received epinephrine, 40.8% ($n = 53/130$) received antihistamines, 3.8% ($n = 5/130$) received β agonists, 29.2% ($n = 38/130$) received corticosteroids, and 15.4% ($n = 20/130$) received no treatment. One in every 5 children presenting with sesame-induced anaphylaxis did not receive epinephrine treatment either in the pre-ED or ED. Four pediatric patients received multiple doses of epinephrine in the ED and no patients were admitted to the hospital (Table 1).

Reactions occurred mainly at home (60.0%; $n = 72/120$), whereas 12.5% ($n = 15/120$) occurred at a school/daycare, 12.5% ($n = 15/120$) in a public location, and 11.7% ($n = 14/120$) in a restaurant. After ED visits, epinephrine autoinjectors (EAI) were prescribed in 67.7% ($n = 88$) of all sesame anaphylaxis cases. Roughly half ($n = 66/130$;

Table 1 (Continued)

Variable (N = 130)	Pediatric patients (n, %)
Pork	2 (1.8%)
Sesame stick	2 (1.8%)
Other (each N = 1/114)	25 (21.9%)
Time until reaction after exposure: (N = 120)	
< 5 min	58 (48.3%)
5 min to < 2 h	56 (46.7%)
2 h to < 8 h ^b	4 (3.3%)
Treatment in the pre-ED setting:	
Epinephrine	42 (32.3%)
Antihistamines	66 (50.8%)
Beta agonists	6 (4.6%)
Corticosteroids	1 (0.1%)
No treatment	39 (30.0%)
Treatment in the ED:	
Epinephrine	62 (47.7%)
Antihistamines	53 (40.8%)
Beta agonists	5 (3.8%)
Corticosteroids	38 (29.2%)
No treatment	20 (15.4%)
No epinephrine treatment pre-ED or in ED	26 (20.0%)
2+ Epinephrine treatment in ED	4 (3.1%)
Hospital admission	0 (0.0%)
Location of reaction: (N = 120)	
Home	72 (60.0%)
School or daycare	15 (12.5%)
Public location	15 (12.5%)
Restaurant	14 (11.7%)
Family or friend's house	4 (3.3%)
Epinephrine autoinjectors:	
Prescribed epinephrine autoinjector	88 (67.7%)
Already has epinephrine autoinjector	31 (24.0%)
Not prescribed an epinephrine autoinjector	35 (26.9%)
Referred to an allergist for evaluation	66 (50.8%)

Abbreviation: ED, emergency department.

^aThe term nut was used when parents did not specify if the nut allergy was to peanut or tree nut.

^bThe 4 reactions occurring from 2 hours to less than 8 hours may be related to late recognition/recall bias or rare cases of delayed anaphylaxis.

Table 2
Factors Associated With Epinephrine Treatment in the Pre-ED

Variable	Univariate (OR, 95% CI)	Multivariate (OR, 95% CI)
Age at reaction	1.01 (0.99–1.02)	1.00 (0.98–1.02)
Sex (male)	1.22 (1.04–1.44) ^a	1.27 (1.08–1.50) ^a
Severe anaphylaxis	0.96 (0.67–1.38)	1.08 (0.77–1.50)
Known food allergy	1.22 (1.03–1.44) ^a	1.36 (1.11–1.68) ^a
Known sesame allergy	1.04 (0.88–1.23)	0.89 (0.72–1.09)
Reaction at home	0.83 (0.71–0.99) ^a	0.92 (0.76–1.11)
Reaction at school	1.29 (1.01–1.66) ^a	1.23 (0.93–1.62)

Abbreviations: CI, confidence interval; ED, emergency department; OR, odds ratio.

^aStatistically significant ($P < .05$).**Table 3**
Factors Associated With Multiple (2+) Epinephrine Treatment in the ED

Variable	Univariate (OR, 95% CI)	Multivariate (OR, 95% CI)
Age at reaction	1.01 (1.00–1.02) ^a	1.00 (1.00–1.02) ^a
Sex (male)	1.04 (0.89–1.22)	1.06 (0.91–1.25)
Epinephrine pre-ED	0.93 (0.74–1.17)	0.87 (0.69–1.11)
Antihistamines pre-ED	1.08 (0.92–1.25)	1.07 (0.91–1.26)

Abbreviations: CI, confidence interval; ED, emergency department; OR, odds ratio.

^aStatistically significant ($P < .05$).

50.8%) of the children were referred to an allergist for evaluation (Table 1).

Factors Associated With Epinephrine Use

In the pre-ED setting, epinephrine was more likely used in boys and patients with a known food allergy after adjusting for age, reaction severity, history of sesame allergy, and reaction location (adjusted odds ratio [aOR], 1.27 [95% confidence interval (CI), 1.08–1.50] and aOR, 1.36 [95% CI, 1.11–1.68], respectively) (Table 2).

In the ED, the likelihood of receiving multiple epinephrine doses increases with age (aOR, 1.00 [95% CI, 1.00–1.02]) when adjusting for sex and pre-ED setting treatments with epinephrine and antihistamines (Table 3).

Discussion

In this decade-long cross-Canada study of anaphylaxis, we identified that sesame-induced anaphylaxis in children is mainly triggered by hummus. Both in the pre-ED setting and ED, epinephrine remains underused. Boys and those with a known food allergy are more likely to receive epinephrine pre-ED, whereas older children are more likely to receive more than 1 epinephrine treatment in the ED. This reinforces the concern that epinephrine is underutilized and not administered promptly enough.

The finding that most reactions follow exposure to hummus may account for the severity of presentation.¹¹ A major ingredient in hummus is tahini, which is made of ground hulled sesame. Tahini often presents as an unknown sesame-containing food to the community, thereby causing many severe sesame allergic reactions.¹² Unlike sesame grains that can move through the gastrointestinal tract unabsorbed, crushed sesame protein in tahini allows for increased absorption.¹³ Oleosin, a seed storage protein of sesame, is found in 2 forms within sesame extracts (Ses i 4 and Ses i 5) and acts as a lipid droplet stabilizer.¹⁴ The oleosin protein family has hydrophobic binding sites for lipid ligands, promoting lipid binding.¹⁴ This protects the sesame allergen from gastrointestinal degradation and aids in intestinal cell uptake.¹⁴ The binding of immunomodulatory lipids causes enhancement of T Helper Cell Type 2 (T_H2) actions and contributes to protein allergenicity.¹⁴ These lipophilic allergenic oleosins contribute to severe allergic reactions as there is increasing evidence that such lipophilic proteins can trigger immune reactions.¹⁵

Table 4
Comparison Between Prospective and Retrospective Patient Data Collection of Pediatric Cases of Sesame-Induced Anaphylaxis

Variable	Prospective	Retrospective
Number of cases	74 (56.9%)	56 (43.1%)
Age at reaction (mean, SD)	5.7 (4.8)	4.1 (5.0)
Sex – male	41 (55.4%)	39 (69.6%)
Sex – female	33 (44.6%)	17 (30.4%)
Reaction severity – moderate	54 (73.0%)	25 (44.6%)
Reaction severity – severe	2 (2.7%)	5 (8.9%)
Epinephrine (pre-ED)	22 (29.7%)	20 (35.7%)
Epinephrine (ED)	33 (44.6%)	29 (51.8%)

Abbreviation: ED, emergency department.

Our findings indicate a substantial underutilization of epinephrine in sesame-induced anaphylaxis, both in the pre-ED and ED setting. Contributing factors to epinephrine underutilization in pediatric patients include no previous allergy diagnosis, epinephrine inaccessibility at the time of reaction, and inability to correctly recognize the child's symptoms.^{16,17} As caregivers often administer EAI to pediatric patients, this can act as a barrier to the EAI administration process.¹⁶ In a study by Chad et al,¹⁸ more than half of the parent participants (55.6%) were fearful of using an EAI on account of hurting the child, incorrect EAI use, or adverse outcomes. To counteract barriers to underutilization, allergists must continue to educate families on the safety and efficacy of EAI and the indications for use. In addition, physicians should help empower parents to use EAI promptly when indicated, which may be facilitated by addressing parental concerns related to EAI use and encouraging parents to practice the proper technique using a trainer during clinical visits.

Furthermore, a delay between sesame ingestion and reaction can also contribute to the underuse of EAI. In our study, nearly half of the sesame-induced anaphylaxis cases (46.7%) occurred between 5 minutes and under 2 hours after ingestion. Thus, parents and guardians may not attribute delayed symptoms to an allergic reaction, especially during a first-time reaction. In addition, it has been reported that only approximately half of patients regularly carry an unexpired EAI.¹⁶ As 40% of sesame-induced anaphylaxis reactions reported herein did not occur at home, patients and parents may not have had an EAI available at the time of reaction. Consistent epinephrine carriage as well as prompt and proper administration must continue to be promoted by physicians to families to manage pediatric sesame anaphylaxis.

Our study reveals that epinephrine was more likely to be used in boys and patients with a known food allergy in the pre-ED setting. Children with known sesame anaphylaxis already have an EAI prescription, which increases the likelihood of epinephrine use on reaction. However, the difference in sex-based epinephrine use is not clear. The sex disparity could be accounted for by various factors, including disproportionately more boys in our study (61.5% boys to 38.5% girls) or a higher EAI prescription rate in boys during childhood.¹⁹ Moreover, a greater prevalence of needle fear was found in female pediatric patients than in their male counterparts, with fear of needles decreasing with increased age in both sexes.¹⁹ Therefore, our findings align with previous research that male pediatric patients exhibit higher trends of epinephrine use in the pre-ED setting.

Our findings reveal that the likelihood of receiving multiple epinephrine doses in the ED increases with age. A second dose of epinephrine is often administered after 5 to 15 minutes in patients with severe anaphylaxis or if there is an inadequate response to the first dose.²⁰ Epinephrine dosage relates to a patient's body weight, with a recommended dosage of 0.01 mg/kg body weight.²¹ Accordingly, older children at higher weights tend to need a higher dosage or 2 dosages of epinephrine because they may be underdosed if using the 0.15 mg autoinjector.²¹ In addition, the average volume of sesame-product eaten in older children is likely higher than in younger

children. Thus, a greater serving-for-age portion of allergen could contribute to a more severe reaction in older patients. A limitation of the study is that data on patients' height, weight, epinephrine dosage, and sesame quantity eaten were not available.

In our study, it was observed that the most common sesame coallergy was peanut (26.9%), followed by nut (15.4%) and tree nut (11.5%). These foods are reported to have high rates of coallergies.²² Pediatric patients with peanut or tree nut allergies are at a greater risk for developing less common food allergies, including sesame.²³ Interestingly, sesame seed storage proteins are also found in peanuts and tree nuts, such as walnuts and Brazil nuts.³ Given the high rate of codiagnosis of peanut and sesame allergies, it may be prudent to evaluate peanut tolerance in patients who have experienced a reaction to sesame.²³

Our study includes several limitations. First, despite being a cross-Canada study consisting of recruitment in 8 Canadian centers (ED + EMS), most patients (91.6%) were recruited from Quebec. Nevertheless, as the sample size is relatively large and patients were recruited from multiple provinces, we believe that our results are still valid. In addition, not all patients with anaphylaxis attend the ED, and data on household income, race, and ethnicity were not collected in this study. Moreover, almost half of the cases were recruited retrospectively (43.1%). However, retrospective and prospective cases were similar regarding demographics, comorbidities, and management (Table 4). Finally, given that challenge tests (skin, oral) were not conducted at all sites, it was assumed that the pediatric sesame allergies led to anaphylaxis with sesame as the trigger.

In conclusion, our findings reveal that sesame-induced anaphylaxis in children often occurs as the first manifestation of sesame allergy and is mainly attributed to hummus ingestion. There is still substantial EAI underutilization, emphasizing the importance of programs to educate patients and families on prompt, safe EAI use. Moreover, physicians and ED staff must promote prehospital EAI use. Thus, as cases of sesame-induced anaphylaxis heighten in Canada, so does the need for ongoing management and awareness in the community.

References

- Clarke A, Elliott S, St Pierre Y, Soller L, La Vieille S, Ben-Shoshan M. Temporal trends in prevalence of food allergy in Canada. *J Allergy Clin Immunol Pract.* 2020;8(4):1428–1430. e5.
- Adatia A, Clarke A, Yanishevsky Y, Ben-Shoshan M. Sesame allergy: current perspectives. *J Asthma Allergy.* 2017;10:141–151.
- Magni C, Ballabio C, Restani P, Fuggetta D, Alessandri C, Mari A, et al. Molecular insight into IgE-mediated reactions to sesame (*Sesamum indicum* L.) seed proteins. *Ann Allergy Asthma Immunol.* 2010;105(6):458–464.
- Gangur V, Acharya H. The global rise and the complexity of sesame allergy: prime time to regulate sesame in the United States of America? *Allergies.* 2020;1(1):1–21.
- Gabrielli S, Clarke A, Morris J, Eisman H, Gravel J, Enarson P, et al. Evaluation of prehospital management in a Canadian emergency department anaphylaxis cohort. *J Allergy Clin Immunol Pract.* 2019;7(7):2232–2238. e3.
- Ruiz J, Zotova V, Ben-Shoshan M, Tariq H, Sheppard T, Asai Y, et al. Cross-Canada Anaphylaxis Registry (C-CARE): comparing rates, triggers, and management of anaphylaxis in a single centre emergency department (ED) over 4 years. *J Allergy Clin Immunol.* 2018;141(2):AB155.
- Sampson H, Muñoz-Furlong A, Campbell R, Adkinson N, Bock S, Branum A, et al. Second symposium on the definition and management of anaphylaxis: summary report—Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *J Allergy Clin Immunol.* 2006;117(2):391–397.
- Muraro A, Roberts G, Worm M, Bilò M, Brockow K, Fernández Rivas M, et al. Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology. *Allergy.* 2014;69(8):1026–1045.
- Gabrielli S, Clarke A, Morris J, Gravel J, Lim R, Chan E, et al. Fruit-induced anaphylaxis: clinical presentation and management. *J Allergy Clin Immunol Pract.* 2021;9(7):2825–2830. e2.
- Inomata N, Osuna H, Yanagimachi M, Ikezawa Z. Late-onset anaphylaxis to fermented soybeans: the first confirmation of food-induced, late-onset anaphylaxis by provocation test. *Ann Allergy Asthma Immunol.* 2005;94(3):402–406.
- Ratnarajah K, Clarke AE, McCusker C, Gabrielli S, Morris J, Gravel J, et al. Anaphylaxis as a presenting symptom of food allergy in children with no known food allergy. *J Allergy Clin Immunol Pract.* 2020;8(8):2811–2813. e2.
- Caminiti L, Vita D, Passalacqua G, Arrigo T, Barberi S, Lombardo F, et al. Tahini, a little known sesame-containing food, as an unexpected cause of severe allergic reaction. *J Investig Allergol Clin Immunol.* 2006;16(5):308–310.
- Achouri A, Boye JL. Thermal processing, salt and high pressure treatment effects on molecular structure and antigenicity of sesame protein isolate. *Food Res Int.* 2013;53(1):240–251.
- Bublin M, Eiwegger T, Breiteneder H. Do lipids influence the allergic sensitization process? *J Allergy Clin Immunol.* 2014;134(3):521–529.
- Schwager C, Kull S, Krause S, Schocker F, Petersen A, Becker WM, et al. Development of a novel strategy to isolate lipophilic allergens (oleosins) from peanuts. *PLoS One.* 2015;10(4):e0123419.
- Glassberg B, Nowak-Węgrzyn A, Wang J. Factors contributing to underuse of epinephrine autoinjectors in pediatric patients with food allergy. *Ann Allergy Asthma Immunol.* 2021;126(2):175–179. e3.
- Lee S, Hess EP, Lohse C, Souza DL, Campbell RL. Epinephrine autoinjector prescribing trends: an outpatient population-based study in Olmsted County, Minnesota. *J Allergy Clin Immunol Pract.* 2016;4(6):1182–1186. e1.
- Chad L, Ben-Shoshan M, Asai Y, Cherkaoui S, Alizadehfar R, St-Pierre Y, et al. A majority of parents of children with peanut allergy fear using the epinephrine auto-injector. *Allergy.* 2013;68(12):1605–1609.
- McLenon J, Rogers MAM. The fear of needles: a systematic review and meta-analysis. *J Adv Nurs.* 2019;75(1):30–42.
- Campbell RL, Kelso JM. Anaphylaxis: emergency treatment. UpToDate. Available at: <https://www.uptodate.com/contents/anaphylaxis-emergency-treatment/print>. Accessed December 23, 2021.
- What are the dosing guidelines for the EpiPen® Auto-injector? Available at: <https://www.epipen.ca/node/25>. Accessed December 23, 2021.
- Brough HA, Caubet JC, Mazon A, Haddad D, Bergmann MM, Wassenberg J, et al. Defining challenge-proven coexistent nut and sesame seed allergy: a prospective multicenter European study. *J Allergy Clin Immunol.* 2020;145(4):1231–1239.
- Stutius LM, Sheehan WJ, Rangsihienchai P, Bharmanee A, Scott JE, Young MC, et al. Characterizing the relationship between sesame, coconut, and nut allergy in children. *Pediatr Allergy Immunol.* 2010;21(8):1114–1118.