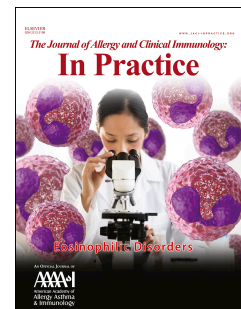


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Using skin prick test to sesame paste in the diagnosis of sesame seed allergy

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Clinical Implications statement: In patients with negative SPTs to both sesame extract and sesame paste, proceeding with a supervised OFC could be recommended. When both SPTs are positive, or positive only to the sesame extract, food avoidance is advisable, especially in patients who present associated atopic dermatitis or allergy to other foods.

Key Words: Sesame, food allergy, skin prick test, tahini, food challenge

TO THE EDITOR:

Allergy to sesame (*Sesamum indicum*) is an increasingly recognized health burden, especially in developed countries like the United States, Japan, and some European nations. Sesame is a major cause of severe IgE-mediated food-allergic reaction among infants and young children in Israel (1, 2). Medical history, skin prick test (SPT) and specific IgE (sIgE) results are frequently used to determine whether an oral food challenge (OFC), the gold standard for diagnosis, is warranted. However, the diagnostic accuracy of both the SPT and sIgE using sesame extract is suboptimal (3, 4). In several reported cases, seed-induced anaphylaxis was proven by challenge tests, in patients with negative SPT reactions and/or sIgE levels (5,6,7). Kanny et al. suggest that the poor sensitivity of sesame tests could reflect paucity of clinically relevant allergens, probably due to a process which removes allergenic lipid derivatives (oleosins) (5). Recently, Appel et al, suggested a stepwise method using basophil activation test (BAT) and SPT with high protein concentration sesame extract (100 mg/ml protein) to obviate the need for OFC in most suspected sesame food allergy (SFA) patients (8). However, the BAT method is time-consuming and expensive. There is evidence that some patients with negative SPTs to both commercial and fresh sesame extract preparations may test positive to SPTs using sesame paste (tahini) or sesame oil (6, 9). Therefore, our aim was to assess the value of adding SPT with sesame paste (tahini) to commercial sesame extract during the evaluation of children with suspected sesame allergy who later performed a sesame oral food challenge. We retrospectively reviewed the medical records of 163 children (median age 24 months, (IQR, 17.5-48)), who underwent OFC to diagnose or rule-out sesame allergy. All participants had a history of previous reaction to sesame. Of the 163 subjects, 41/160 had asthma (25.6%), 63/160 had atopic dermatitis (39.3%) and 67/147 (45.5%) reported other food allergies. All children underwent skin prick testing with commercial sesame extract and 123 (75.4%) also underwent a skin prick test with sesame paste (We utilized ACHVA, a commercial based- product, containing 240 mg protein/ gram). Wheals with a mean diameter ≥ 3 mm greater than the negative control were considered positive reactions. An oral food challenge to sesame was performed using tahini paste (240 mg protein/ gram) or halva by introducing increasing doses from 20 mg protein through 50 mg, 100 mg, 200 mg, 400 mg, 800 mg, 1.2 gram, 2 grams, and in older children 4 grams every 20–30 min, with a 120-minute observation period following the final dose. Patients

70 who showed no reaction during the OFC were considered tolerant if no allergic symptoms
 71 appeared after ingesting sesame at home for one week. We used this protocol since patients may
 72 react several days after ingesting this allergen. Chi-square analysis or Fisher's exact test for
 73 discrete variables were used for descriptive analysis of differences between the groups. Receiver
 74 operating characteristic (ROC) analysis was used to evaluate the sensitivity and specificity of
 75 commercial sesame extract and tahini paste in skin prick testing for the diagnosis of sesame
 76 allergy. Logistic regression analysis was used to assess the association between the variables of
 77 interest and subsequent positive sesame oral food challenge. The level of significance was set at
 78 $p \leq .05$. Sixty (36.8%) of the patients had a positive reaction to the food challenge and therefore,
 79 were considered to have sesame allergy. The demographic and clinical manifestation differences
 80 between patients with and without SFA are presented in Table 1. The sensitivity, specificity,
 81 positive predictive value (PPV) and negative predictive value (NPV) of using SPT with
 82 commercial extract and tahini paste in detecting sesame allergy are presented in Table 2. The
 83 findings indicate that tahini paste, which is generally easy to obtain and inexpensive, increased
 84 the sensitivity of the SPT from 33.3% with the commercial extract to 86.7%, and reduced the
 85 specificity of the test from 86.4% to 52.6%. The combined tests yield a sensitivity of 68.4% and
 86 a specificity of 86.4%, PPV of 59.1% and NPV of 87%, ROC analysis yielded an area under the
 87 curve (AUC) of 0.66 (95% confidence interval: 0.56%-0.76%) for the commercial extract, and
 88 0.77 (95% confidence interval: 0.68%-0.85%) for the tahini paste, demonstrating an
 89 improvement of the tahini paste over the commercial extract at 0.71 (Diff: 0.1 (0.03-0.174),
 90 $p=0.004$), and suggesting that this approach offers a simple-to use tool to improve sesame allergy
 91 evaluations. Our results showed that 63.2% of the patients successfully passed the food
 92 challenge. This finding suggests that the chances of acquiring tolerance to sesame are higher than
 93 in the case of allergies to tree nuts and peanuts, and lower than for allergies to cow's milk or
 94 eggs. Risk factors for positive sesame food challenge were respiratory manifestation at the initial
 95 reaction to sesame, atopic dermatitis and coexistence of allergy to other foods. However, a
 96 logistic regression predicting positive sesame food challenge in all children revealed a significant
 97 positive association with atopic dermatitis (OR, 2.98; 95% CI, 1.46-6.1; $p=0.003$) and allergic
 98 reactions to other foods (OR, 2.19; 95% CI, 1.08-4.45; $p=0.03$) but not to respiratory
 99 manifestation at the initial reaction. In comparison to Appel et al, study, our sample was
 100 significantly larger, included primarily children and utilized an easy- to- use readily available

commercial sesame product that is simply refrigerated after opening. Several study limitations should be noted. While it may have been interesting to measure sIgE levels we opted to rely on SPT alone since previous studies have shown that sIgE does not yield additional information. Also, in some cases, a positive history of sensitivity to other food allergens was elicited only by parental report. Finally, we did not assess all allergens that might be significant in the diagnosis of SFA in this population, such as oleosins. Of note, tahini paste may have a relatively low specificity and PPV since it may contain proteins that are degraded in the digestive tract thereby eliciting a limited perioral reaction e.g., redness/mild oral tingling without a systemic allergic response. Until more innovative, easy-to-perform methods are developed, we suggests that suspected sesame allergy be assessed by SPT with both commercial extract and tahini paste. These findings may help the clinician, in some cases, to estimate outcomes of OFC more accurately. In cases where both SPT are negative, we recommend proceeding with an OFC in a medical setting. With regard to patients with positive SPT to sesame commercial extract and paste, or only positive to sesame commercial extract, we typically continue with food avoidance, especially in cases with additional underlying risk like atopic dermatitis and other food allergies. Approximately half of the patients with only a positive SPT to sesame paste will tolerate a sesame OFC. If there are no additional aforementioned risk factors, our group would attempt the challenge in a hospital setting.

References

1. Dalal I, Goldberg M, Katz Y. Sesame seed food allergy. *Curr Allergy Asthma Rep* 2012;12:339e45.
2. Dalal I, Binson I, Levine A, Somekh E, Ballin A, Reifen R. The pattern of sesame sensitivity among infants and children. *Pediatr Allergy Immunol* 2003;14:312-316.
3. Zavalkoff S, Kagan R, Joseph L, St-Pierre Y, Clarke A. The value of sesame-specific IgE levels in predicting sesame allergy. *J Allergy Clin Immunol* 2008;121(6):1508-1510.
4. Eberlein-Konig B, Rueff F, Przybilla B. Generalized urticaria by sesame seeds with negative prick test results and without demonstrable specific IgE antibodies. *J Allergy Clin Immunol* 1995;96:560-561.
5. Kanny G, De Hautecloucque C, Moneret-Vautrin DA. Sesame seed and sesame seed oil contains masked allergens of growing importance. *Allergy* 1996;51:952e957.
6. Della-Torre E, Pignatti P, Yacoub MR, Sabbadini MG, Colombo G. In vivo tests with “Tahini” sauce: new allergenic source to evaluate IgE-mediated hypersensitivity to sesame. *Ann Allergy Asthma Immunol* 2013;110:209-210.
7. Leduc V, Moneret-Vautrin DA, Tzen JT, Morisset M, Guerin L, Kanny G. Identification of oleosins as major allergens in sesame seed allergic patients. *Allergy* 2006;61:349-56.
8. Appel MY, Nachshon L, Elizur A, Levy MB, Katz Y, Goldberg MR. Evaluation of the basophil activation test and skin prick testing for the diagnosis of sesame food allergy. *Clin Exp Allergy* 2018;48(8):1025-1034.

- 148 9. Adataia A, Clarke AE, Yanishevsky Y, Ben-Shoshan M. Sesame allergy: current perspectives.
149 J Asthma Allergy 2017;10:141-151.

TABLE I. The Demographic and clinical characteristics of study participants (n = 163)

	Positive sesame Oral challenge n=60	Negative sesame Oral challenge n=103
Age at OFC (month), median (IQR)	26.5 (20-55.5)	23 (16-42)
Gender, %		
Female	15	38
Male	45	65
Atopic Dermatitis,% (n)	56.7% (34/60)*	28.1% (29/103)
Asthma, % (n)	25.4% (15/59)	24.7% (25/101)
Other food allergy,% (n)	59.3% (35/59)*	35.2% (31/88)
Age at initial reaction to sesame (month) ,median (IQR)	7.0 (6-11)	6.25 (6-8.75)
Allergic manifestations at the time of initial sesame allergy event		
Skin	88.3% (53/60)	90.2% (93/103)
Gastrointestinal	10.0% (6/60)	10.6% (11/103)
Respiratory	11.6% (7/60)*	2.9% (3/103)
Anaphylaxis	1.6% (1/60)	0.97% (1/103)

OFC, oral food challenge; IQR, interquartile range; *P<0.05; Numbers may not add up to total because of missing data.

TABLE II. The diagnostic performance of sesame allergy comparing skin prick test with commercial sesame extract, sesame paste and a combination of the two.

	Sesame commercial extract	Sesame paste (tahini)	Sesame commercial extract and Sesame paste*	Negative sesame commercial extract and positive sesame paste
Sensitivity	33.3%	86.7%	68.4%	57.8%
(95% CI)	(21.4-45.2)	(76.8-96.6)	(47.5-89.3)	(43.4-72.2)
Specificity	86.4%	52.6%	86.4%	64.1%
(95% CI)	(79.8-93.0)	(41.5-63.7)	(70.8-92.5)	(53.5-74.7)
PPV	58.8%	51.3%	59.1%	48.1%
(95% CI)	(42.3-75.3)	(40.1-62.5)	(38.6-79.7)	(34.8-61.4)
NPV	69.0%	87.2%	87.0%	72.5%
(95% CI)	(61.0-77.0)	(77.7-96.8)	(77.3-96.7)	(58.1-86.9)

CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.

* Cases where both SPTs were negative or positive.