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Anaphylaxis Associated with Peanuts and Nuts in Late Mexican Adolescents: A Population Based Study

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Abstract

Background: There is a lack of information regarding anaphylaxis that is triggered by the peanut and nuts in countries with emerging economies. We aimed to identify the factors that are related to the prevalence of secondary anaphylaxis that results from ingesting peanuts or nuts.

Materials and Methods: A cross-sectional, population-based study was conducted in which we applied a structured questionnaire to a random sample of 1992 adolescents, aged 15 to 18 years. After identifying those subjects with presence of adverse symptoms after food intake, we then asked if this was due to the ingestion of the peanuts or nuts. Factors associated with anaphylaxis were identified through the odds ratio estimation using logistic regression in a multivariate analysis model.

Results: The prevalence of global anaphylaxis caused by the peanuts and nuts was 0.9%, n=17 (95% CI: 0.5% to 1.4%); 0.6%, n=12 (95% CI: 0.3% to 1.1%) with any type of nut, and 0.3%, n=7 (95% CI: 0.2% to 0.7%) with the peanut; anaphylaxis caused exclusively by the peanut was recorded at 0.2% (95% CI: 0.1% to 0.6%). Notably, one case of anaphylaxis was triggered by five types of nuts (almond, pecan, Brazilian nut, cashew, and pistachio), another by 4 types (hazelnut, peanut, walnut, pecan, and cashew), there were 9 cases that were prompted by only one food (5 peanut, 2 cashew, 1 chestnut, 1 almond). The only factor found to be associated with anaphylaxis was a personal history of pollen allergy, odds ratio: 10.12 (p = 0.046).

Conclusion:
The prevalence of anaphylaxis induced by peanuts or nuts in the Mexican population varies from 0.5 to 1.4%; and the personal history of pollen allergy was the only associated factor with anaphylaxis.

Key Words: Anaphylaxis, Adolescents, Allergy, Prevalence.

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1- INTRODUCTION

Anaphylaxis is primarily triggered by foods, drugs, or insect bites, however, the frequency with which this occurs varies with age; in children foods are the main culprit; with adults, drugs are the main factors (1). Although several foods may cause anaphylaxis, peanuts, nuts, and seafood are the primary sources among children and adults; yet, in the case of infants that are breastfed, milk and eggs are more frequently associated with its occurrence (2). The increased consumption of nuts and seeds during the last decades have likely caused a higher frequency of sensitization to them, which is why fatal and near-fatal reactions are becoming more common (3). The prevalence of sensitization and allergy to nuts varies throughout geographic regions; overall, the food allergy ranges from 5.2 to 35% (4).

The data gathered in European and North American countries concludes that the walnut and the hazelnut occupy first place amongst fruit and seed allergies. The general sensitization prevalence to these foods varies from 1 to 12%, and these types of reactions comprise 8 to 10% of all emergency room visits that result from food ingestion (3, 5, 6). Various risk factors have been attributed to anaphylaxis, age is among the most noted factor, as it is more common during childhood; other related aspects include a family history of allergy, sex, and sensitization to pollen (4,7-10).

In countries with emerging economies, such as Mexico, there is a need to understand the dimension of anaphylaxis and its relation to the ingestion of peanut and nuts. Given that the available evidence pertaining to this matter is incredibly scarce, especially amongst the adolescent population aged 15 to 18 years, for which there are no previous studies to reference; our objective was to identify the factors that are associated with the prevalence of anaphylaxis due to the consumption of peanuts and nuts amongst late Mexican adolescents.

2- MATERIALS AND METHODS

2-1. Ethics

The Hospital Ethics Committee of Research approved and supervised this project. After presenting the objective of our study, the authorities and teachers from each of the schools that participated in our project gave their consent and helped with the application of the questionnaires amongst the adolescents; all adolescents were asked to give verbal consent prior to their participation.

2-2. Setting

The city of Guadalajara is located in western Mexico and, together with its metropolitan area, it is considered the second largest city in our country. There are almost 1.5 million inhabitants within its geographic area and its constituents comprise all socioeconomic levels. The people habitually consume typical food of the region derived from corn, beans, peppers, as well as, pork, beef and goat meat (11).

2-3. Design and Sample

A cross-sectional, population-based study was conducted. This is a secondary analysis of a study whose methodology has been previously described (12); during which we analyzed data that corresponded to 1992 late adolescents (aged 15 to 18 years); all participants came from public and private schools. Data were gathered from April to June of 2016. The students were selected through stratified and cluster sampling. Since our host city is divided into 7 administrative districts (or strata), we selected at least one school cluster from each stratum; proportionally, each stratum also provided a student sub-sample. Therefore, each school grade was considered as a new cluster, and we selected a random group from each of

these. Finally, we pooled students to participate in our survey through random selection.

2-4. Questionnaire

When attempting to identify anaphylaxis triggered by the peanuts or nuts, we applied a structured questionnaire to each participating adolescent with questions regarding their age, and sex, as well as their personal and family history of allergic diseases. The question: *Do you suffer from allergic reactions after eating foods?* Allowed us to identify the presence of adverse symptoms after the ingestion of foods (13). When participants answered affirmatively, we then asked if this was due to the ingestion of the peanuts or nuts (almond, hazelnut, chestnut, Brazilian nut, cashew, macadamia, and pistachio), furthermore, we inquired as to how long it took for these symptoms and discomfort to take effect after their intake. An anaphylactic reaction caused by peanuts or nuts was defined as the affection of two or more organs or systems, with symptoms of typical allergic reactions like hives or angioedema, difficulty in breathing, wheezing, chest tightness, vomiting or diarrhea, within the first two hours after the intake of these particular food items (14). A pollen allergy was defined when there was an affirmative answer to the question: *Are you allergic to pollen*? A copy of the food allergy questionnaire can be obtained online (13).

2-5. Analysis

When comparing categorical variables, we used the chi-square test or Fisher's exact test; for continuous variables we employed the Student's *t*- test. 95% confidence intervals (95% CI) were estimated for proportions according to the Central Limit Theorem or the binomial distribution as appropriate. The *p*- value ≤ 0.05 was considered statistically significant. We identified factors associated with anaphylaxis triggered by peanuts and nuts through logistic regression, by doing so, we compared individuals with an allergy to peanuts and nuts that did not manifest anaphylaxis to those who were also allergic to the peanuts and nuts but did manifest anaphylaxis. The data was analyzed by using the SPSS Statistics program 20.0 version (IBM Co., Armonk, NY, USA) for Windows.

3- RESULTS

Amongst 1992 adolescents, 27 (1.4%; 95% CI: 0.9% to 2.0%) reported some type of adverse reaction after having ingested peanuts or nuts (1.4%; 95% CI: 0.9% to 2.0%). Of these 27, 17 had symptoms that suggested an anaphylactic reaction (0.9%; 95% CI: 0.5% to 1.4%). Notably, none of the cases had been previously diagnosed by a physician as anaphylactic reactions. The mean age of the adolescent group with anaphylaxis was significantly lower in relation to those who did not manifest the symptom (16.3 ± 0.8 years vs. 17.0 ± 0.8 years, p=0.045) (**Table.1**). The frequency of a pollen allergy was greater among students with anaphylaxis (52.9% vs. 10.0%, p=0.042). There was no significant association between a personal or family history of an atopic disease or exercise regularity with an anaphylactic reaction. Cutaneous and respiratory discomfort stood out among patients with an anaphylactic reaction in the following order of decreasing frequency: skin reddening, wheezing, bodily itchiness, hives, sneezing, nasal congestion and rhinorrhea **(Table.2)**.

Based on the food, the prevalence of anaphylaxis caused by any nut was 0.6% (95% CI: 0.3% to 1.1%), for peanut it was 0.3% (95% CI: 0.2% to 0.7%), anaphylaxis exclusively associated with peanut was 0.2% (95% CI: 0.1% to 0.6%) **(Table.3)**. Nuts with a reduced prevalence were the Brazilian nut, hazelnut, cashew, chestnut and pistachio. **Table.4** displays the clinical characteristics of the 17 individuals with

anaphylaxis caused by peanuts or nuts. Overall, there was a similar number of affected men and women (41%, and 59%, respectively). 12 of the 17 cases (70%) had a personal history of atopic disease; the most common were asthma and allergic rhinitis. One student reported that 5 nuts triggered his anaphylaxis (almond, walnut, macadamia, Brazilian nut, cashew and pistachio); another individual mentioned 4 foods (hazelnut, peanut, macadamia and cashew), while another listed 3 (almond, peanut, and the Brazilian nut); there were five cases caused by two nuts (4 by almonds and the macadamia, one by the almond and the hazelnut). There were 9 (0.5%) total cases that were only allergic to one nut or seed, 5 of which were the peanut, 2 macadamias, 1 hazelnut and 1 almond). According to multivariate analyses, the only factor associated with anaphylaxis triggered by peanuts or nuts was a pollen allergy (odds ratio [OR]: 10.12; p = 0.046) **(Table.5)**.

Table-1: Characteristics of the population with some type of adverse reaction associated with the intake of peanuts or nuts

Variables	Anaphylaxis		P-value
	Yes n = 17	No n = 10	
Age, years ± SD	16.3 ± 0.8	17.0 ± 0.8	0.045
Gender (%)			
Male	7 (41.2)	3 (30.0)	0.692
Female	10 (58.8)	7 (70.0)	
Pollen allergy (%)	9 (52.9)	1 (10.0)	0.042
Exercise (%)	15 (88.2)	9 (90.0)	0.999
Personal history of atopic disease (%)			
Asthma	8 (47.1)	2 (20.0)	0.230
Allergic rhinitis	9 (52.9)	5 (50.0)	0.883
Atopic dermatitis	5 (29.4)	1 (10.0)	0.363
Familiar history of atopic diseases (%)			
Mother			
Asthma	3 (17.6)	1 (10.0)	0.999
Allergic rhinitis	4 (23.5)	1 (10.0)	0.621
Atopic dermatitis	2 (11.8)	0 (0)	0.516
Father			
Asthma	0 (0)	0 (0)	---
Allergic rhinitis	3 (17.6)	0 (0)	0.274
Atopic dermatitis	0 (0)	0 (0)	---

A p-value obtained by one of the following tests as applicable: t-Student, Chi-square, or Fisher exact.

Table-2: Frequency of symptoms in patients with some type of adverse reaction associated with the intake of peanuts or nuts

Symptoms	Anaphylaxis		P-value
	Yes n = 17	No n = 10	
Skin reddening	15 (88.2)	0 (0)	< 0.0001
Wheezing	13 (76.5)	0 (0)	< 0.0001
Body itching	12 (70.6)	1 (10.0)	0.004
Hives	11 (64.7)	1 (10.0)	0.014
Sneezing	10 (58.8)	1 (10.0)	0.018
Nasal congestion	9 (52.9)	0 (0)	0.009
Rhinorrhea	7 (41.2)	0 (0)	0.026

Edema of the lips		7 (41.2)	3 (30.0)		0.692
Cough		6 (35.3)	0 (0)		0.057
Vomiting		6 (35.3)	0 (0)		0.057
Edema of the face		5 (29.4)	1 (10.0)		0.363
Abdominal pain		5 (29.4)	2 (20.0)		0.678
Abdominal bloating		3 (17.6)	2 (20.0)		0.999
Diarrhea		2 (11.8)	0 (0)		0.516
P-value obtained by Fisher's square or exact Chi-square test.					

Table-3: Prevalence of anaphylaxis according to type of food in 1992 students

Type of food		Number	%	95% CI
Any nut		12	0.6	0.3 a 1.1
Peanut		7	0.3	0.2 a 0.7
Only peanut		5	0.2	0.1 a 0.6
Almond		8	0.4	0.2 a 0.8
Pecan		8	0.4	0.2 a 0.8
Brazil nut		2	0.1	0.01 a 0.4
Hazelnut		2	0.1	0.01 a 0.4
Indian nut		2	0.1	0.01 a 0.4
Chestnut		1	0.05	0.00 a 0.3
Pistachio		1	0.05	0.00 a 0.3
95% CI: 95% confidence interval.				

Table-4: Characteristics of subjects with anaphylaxis triggered with peanuts and nuts

Case	Age	Gender	Personal history	Food type							
				Almond	Hazelnut	Peanut	Chestnut	Pecan	Brazil nut	Indian nut	Pistachio
1	17	M	AR					+			
2	17	F	BA, AR					+			
3	17	F	---			+					
4	17	F	AD	+							
5	17	F	BA, AR			+					
6	17	F	BA, AR, AD			+					
7	16	M	---				+				
8	15	F	AR			+					
9	16	M	---			+					
10	16	M	BA, AR	+				+			
11	15	F	BA, AR, AD	+				+			
12	16	M	---	+				+			
13	15	F	BA, AR, AD	+				+			
14	16	M	---	+	+						
15	16	M	BA, AD	+		+			+		
16	16	F	AD		+	+		+		+	
17	17	F	BA, AR	+				+	+	+	+

M: male; F: female.
BA: bronchial asthma; AR: allergic rhinitis; AD: atopic dermatitis.
(+): positive; (-): negative.

Table-5: Factor associated with anaphylaxis triggered by peanuts or nuts

Variables	Non-adjusted model			Adjusted model		
	OR	95% CI	P-value	OR	95% CI	P-value
Age	0.41	0.09 – 1.97	0.268	---	---	0.166
Pollen allergy	9.08	0.55 – 148.79	0.122	10.12	1.04 – 98.49	0.046
Sex, male	3.43	0.28 – 41.90	0.334	---	---	0.190
Exercise	1.45	0.022 – 98.31	0.862	---	---	0.660
Asthma	3.60	0.31 – 42.52	0.308	---	---	0.275
Allergic rhinitis	1.48	0.10 – 22.87	0.777	---	---	0.884
Atopic dermatitis	3.65	0.05 – 282.59	0.560	---	---	0.965

OR obtained by binary logistic regression. All variables were introduced dichotomously except for age which was introduced continuously. 95% CI: 95% confidence interval.

4- DISCUSSION

To our knowledge, this is the first time that a study focused on determining the prevalence of anaphylaxis triggered by the peanuts or nuts amongst late adolescents has been attempted in our country, and the prevalence was found to be 0.9%. This study also shows that the almond, macadamia and peanut are the foods most frequently linked to anaphylaxis. The only factor associated with anaphylaxis was a personal history of pollen allergy. Many report much higher prevalence of peanut anaphylaxis in the US (0.8-2.1%), Canada and the United Kingdom (15-18). In Mexico a 4-city survey which included 1126 adults (aged 18 to 50 years), reported 15 anaphylactic reactions linked to foods; 2 of these were triggered by peanut (0.2%), one by sesame seed and the other by linseed (0.09% each) (19). In another survey comprising 1200 university students, there were only two cases of symptoms compatible with anaphylaxis triggered by foods (0.2%), one was caused by walnut (0.1%) and the other by cashew and walnut (0.1%) (20). Currently, we do not have an explanation regarding the prevalence associated with peanuts and nuts in industrialized nations or in our own country; yet, it is worthy to note that our country is neither a mass producer nor consumer of peanuts, perhaps something similar could be found pertaining to nuts. The peanut and nut allergy represent a health risk in our population on a frequently occurring basis, and public health officials are not addressing the issue in a satisfactory manner. Surprisingly, none of the cases that we identified throughout this project had been previously diagnosed as anaphylaxis by any other physician, thus not only is this issue under-diagnosed, it is obvious that the treatments offered for these types of problems are inadequate. Furthermore, in our country self-injecting adrenaline is not available; as a result, allergy specialists that treat anaphylaxis are forced to seek alternative methods to provide their patients with adrenaline. Although there is no universally accepted definition for anaphylaxis, the World Allergy Association defines it as: "A generalized hypersensitive reaction or a severe systemic reaction that puts a life at risk" and "an acute allergic reaction that appears suddenly, and can lead to death", in which two or more organs or systems are affected (7). The frequency with which discomfort is triggered varies according to age; in those under 6 years of age, intestinal symptoms are more common, however during school-age and adolescence, respiratory discomfort is more frequent, whereas adults tend to present symptoms

of hypotension and a cardiovascular nature (10). In our study, the most common discomfort found in adolescents was cutaneous, followed by respiratory, and lastly intestinal, which appears to be the generally observed pattern in Latin American populations (21, 22). Out of the 27 patients that reported being allergic to the peanuts and nuts in our study, 63% of them had had an anaphylactic reaction; thus, we recommend carefully questioning patients with an allergy to such foods. When there are systemic symptoms that are compatible with anaphylaxis, individuals should avoid certain foods, according to the severity of their reactions, furthermore, when necessary, the physician must instruct the patient to self-administer adrenaline. The peanut is a seed that belongs to the legume group; soy, beans, peas and others also belong to this family. This means that there is a likely association with nuts; out of 7 of the anaphylactic cases that were triggered by peanuts, two (28.6%) had coexisting allergies to nuts that were not taxonomically related; this number is consistent with previous reports, where 20% to 40% of individuals behave this way (23). However, because we did not carry out any tests to confirm allergies, this percentage could vary considerably. In the case of nuts, out of 8 anaphylaxis cases caused by the pecan nut (Carya genus), one of these was associated with the Brazilian nut (Bertholletia genus), another was linked to the cashew (Aleurites genus), and the Brazilian nut, which would make a mixed reaction unlikely (24). Risk factors for anaphylaxis such as age and co-morbidity when interacting with other coexisting aspects can produce a synergistic anaphylactic effect (7). In this study, we found that students that manifested anaphylaxis triggered by peanuts or nuts were slightly younger in age, in contrast, a personal or family history of asthma, allergic rhinitis or atopic dermatitis were not linked to their reactions. In addition, the prevalence of anaphylaxis may also vary according to age; overall, children are at a greater risk of having an anaphylactic response than adults are (10). Where atopy is concerned, a cohort study found that Swedish males, aged 16, were 5, 10, and 13 times more likely to manifest anaphylaxis when the individual also had a personal history of asthma, allergic rhinitis or atopic dermatitis, respectively. In our own study, a family history of allergy increased the risk more than twofold (9); in a population of young Mexican adults, a personal history of asthma increased the likelihood of allergy to nuts or peanuts 9 and 5 times, respectively (4); it is likely that we were unable to observe this predisposition, since students with and without anaphylaxis stated that they were allergic to nuts and peanuts, both of these are regulated by Immunoglobulin E, which might cause said reaction (25). Although we did not inquire about it directly, it has been noted that sex hormones play a role in the development of anaphylaxis (8); during our study, we inferred that this was not the case, since the multivariate analyses did not register sex as an associated factor. In Portugal, a recent study carried out among children and adults found no link between anaphylaxis and sex (26). Notably, we established that a pollen allergy is a factor that is strongly tied to anaphylaxis associated with the ingestion of peanuts and nuts; similar findings have been made in Sweden, where adolescents with sensitization to aeroallergens were 10 times more likely to develop asthma; a mixed reaction between proteins that come from pollens and nuts could explain this occurrence (9).

4-1. Limitations of the study

It is important to note that our study lacked tests that allowed us to corroborate an anaphylactic diagnosis, which is why we utilized the questionnaire in order to identify the symptoms that are frequently

related to this reaction, this should be taken into consideration when interpreting our results. We were also unable to verify an allergy to peanuts or nuts through an oral food challenge, despite this method being used as a golden standard for diagnosing food allergies; as it is difficult to conduct in population studies. We also advise caution when trying to generalize our results, in spite of the fact that our study was population based, we only included adolescents from an industrialized city. Rural areas or those far away from our location might have different results, as habits and customs in food intake, as well as food availability can vary considerably. Although it is true that estimating the prevalence of anaphylaxis associated with peanuts and nuts ingestion based on questionnaires can lead to overestimation, one of the benefits of our study is that it can help shed light on a health problem that affects the general population, which has seldom been taken into consideration in countries with developing economies; furthermore, our approach was specific, and targeted peanuts and nuts as a way of avoiding the generalization of all foods. Finally, adolescents probably do not remember their medical history accurately (recall bias); however, if the nature of the disease is taken into account, we consider that adolescents are capable of recognizing their own aliments; if they were not able to know their own disease, nor their own medical history, this sub-registry would be shown in all study subjects, so if there is bias, it would be a non-differential error, which has less impact on distortion of results than a differential error. Likewise, we consider that surveying the parents would be a secondary source for obtaining the data, and that it is not the best strategy due to the possibility that the parents are completely unaware of the child's illness, on the assumption that they are not living with the child (for example, separated parents, stepfather, among other things).

5- CONCLUSION

In closing, we found that the prevalence of anaphylaxis in late adolescents identified in this study (between 0.5% and 1.4%) is similar to that which has been reported in industrialized nations. Nuts such as almond, macadamia, or peanut, were amongst the main factors that caused this type of reaction.

6- CONFLICT OF INTEREST: None.

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