Oral food challenge: a Brazilian panorama

Teste de provocação oral com alimentos: o panorama brasileiro

Lucila Camargo Lopes de Oliveira1,2, Jackeline Motta Franco3,4, Ana Carolina Rozalem Reali1, Ana Paula Beltran Moschione Castro1,5, Ariana Campos Yang1,6,7, Bárbara Luíza de Britto Cançado1, Fabiane Pomiecinoki Frota1, Germana Pimentel Stefani1, Ingrid Pimentel Cunha Magalhães Souza Lima1, José Carlson Santos de-Oliveira1, José Luiz Magalhães Rios1, Nathalia Barroso Acataassú Ferreira1, Renata Rodrigues-Cocco1,8, Valéria Botan-Gonçalves1, Norma de Paula M. Rubini9, Emanuel Sarinho10, Dirceu Solé2,11

ABSTRACT

Background: Oral food challenge (OFC), the gold standard for diagnosing food allergy and determining tolerance levels, requires specialized staff and appropriate conditions since anaphylaxis may occur. In 2022, OFC was officially recognized in Brazilian public and private health systems, although only for milk allergy in children up to 24 months of age. Little is known about OFC practices in Brazil. Objectives: To explore OFC practices, barriers, and solutions among Brazilian allergists and immunologists. Methods: A survey was e-mailed to 2500 associates of the Brazilian Association of Allergy and Immunology regarding OFC practices, training experiences, barriers to this procedure, and workable solutions. Results: A total of 290 associates responded (11.6%), more than a half of whom (56.15) practiced in the southeast region: 158 (54.5%) reported performing OFC, of whom 62% performed > 5 procedures each month, mostly for cow milk and hen egg. OFCs were mostly performed in private practice and were associated with specialized training. Lack of an appropriate setting was seen as the main barrier to performing the procedure.

RESUMO

Introdução: O teste de provocação oral (TPO) com alimentos é o padrão ouro para avaliação diagnóstica e de aquisição de tolerância em pacientes com alergia alimentar (AA). Exige, no entanto, equipe especializada e local apropriado para execução, uma vez que reações alérgicas, incluindo anafilaxia, podem acontecer. Foi recém-incorporado como procedimento reconhecido pelo Sistema Único de Saúde e pela Agência Nacional de Saúde, mas apenas no contexto da alergia ao leite de vaca para pacientes com até 24 meses de vida. Pouco se sabe sobre sua disponibilidade/execução no território brasileiro. Objetivos: Explorar o perfil de realização de TPO com alimentos em âmbito nacional, bem como as limitações para a sua não realização. Métodos: Inquérito virtual foi disponibilizado por e-mail aos 2.500 sócios da Associação Brasileira de Alergia e Imunologia questionando sobre a prática de TPO, formação do profissional, limitações para sua execução e possíveis soluções para sua realização. Resultados: Foram obtidas 290 respostas (11,6% dos associados), sendo a maioria deles proveniente da Região Sudeste (56,1%). Realizam
Conclusions: Although this study’s methodology involves intrinsic biases, this is the first exploration of OFC practice in Brazil. OFCs are still underperformed nationwide.

Keywords: Food hypersensitivity, diagnosis, prognosis, food.

Introduction

The worldwide prevalence of food allergy (FA) is estimated to range from 1% to 10%, affecting people of different ages, ethnicities, and socioeconomic conditions.\(^1\) Approximately 30% of children with FA may experience reactions to multiple food allergens.\(^2\) Data on the prevalence of FA in the Brazilian population are scarce. A national multicenter study observed high sensitization rates, mainly to cow’s milk (84.2%) and egg (70.5%), in a selected population with a medical diagnosis of FA.\(^3\) It also showed a significant increase in sensitization to cow’s milk, peanuts, and corn from 2004 to 2016.\(^3,4\)

The symptoms of FA are nonspecific, and laboratory tests alone are not sufficient to confirm or exclude the diagnosis. The oral food challenge (OFC) is still considered the diagnostic gold standard for FA when performed in a double-blind, placebo-controlled manner.\(^5\) The OFC is also used to investigate acquisition of tolerance to food allergens, which can happen spontaneously or be induced (immunotherapy).\(^5\) However, it needs to be performed in a specialized setting by a trained professional, as it poses a risk of anaphylaxis, a potentially fatal allergic reaction.\(^6-8\) Elimination diet remains the cornerstone of FA management, which may imply nutritional risk, especially for patients with allergies to multiple food allergens.\(^9\) Therefore, a thorough investigation is essential to avoid misdiagnosis and thereby prevent the implementation of unnecessary diets, which reduce quality of life.\(^10\) The OFC is associated with better QoL independent of challenge outcome because it elucidates some aspects of the FA.\(^11\)

Of note, the OFC has only been covered by the Brazilian Unified Health System (Sistema Único de Saúde, SUS) and private health insurances (Brazilian Hierarchic Code of Medical Procedures/TUSS code 2.01.01.36-8) since 2022, and only for children aged up to 24 months in need of diagnosis and/or monitoring of allergy to cow’s milk.\(^12,13\)

Considering the increase in the prevalence of FA in recent decades, as well as the incipient inclusion of the OFC in private and public health systems and its complexity, it is likely that the test is insufficiently performed in Brazil. With the objective of describing the profile of OFC performance in Brazil, including barriers, the Scientific Department of Food Allergy of the Brazilian Association of Allergy and Immunology 2021-2022 (ASBAI) conducted a survey on the topic to be answered by ASBAI members.

Methods

This was a cross-sectional study that assessed OFC performance by allergists and immunologists. Participants answered an on-line questionnaire on Google Forms\(^\text{®}\) (Annex 1).

All 2,500 ASBAI members received an institutional e-mail between June and December 2022 inviting them to participate in the survey, with a link to the questionnaire and the informed consent form. The 15 members of ASBAI’s Scientific Department of Food Allergy were excluded from the survey to avoid bias.
The study was approved by the research ethics committee of Universidade Federal de São Paulo under no. 5.421.086 (0241/2022).

Categorical variables were expressed as frequencies and proportions and compared using Fisher’s exact test. Statistical analyses were performed using Epi Info 7.2.5.0.

**Results**

One of the respondents did not provide informed consent and was excluded from the study. A total of 290 respondents (11.6%) were included, of whom 96.9% had completed medical residency or a fellowship program in Allergy and Immunology, and 45.5% of them had finished their residency/fellowship at least 10 years ago. Education-related characteristics, such as time since residency/fellowship completion and OFC training during residency/fellowship, are presented in Table 1 in relation to whether or not OFC is offered in clinical practice. In our sample, 106 physicians (36.5%) did not perform OFC during residency/fellowship, of whom 40 (37.7%) had completed their education in the last 19 years.

Not offering OFC in clinical practice was statistically higher in the group of physicians who completed their residency/fellowship between 20 and 29 years ago. Those who performed OFC during their medical education were more likely to offer OFC in current clinical practice (p < 0.01), especially if 6 or more OFCs were performed (Table 1).

Figure 1 shows the distribution of respondents according to the state where they work. Three physicians reported working in more than 1 state. Most respondents (n = 158 [54.5%]) reported offering OFC in current clinical practice, especially in the private sector (Figure 2). Just over 62% of these professionals perform up to five OFC with food monthly, and almost 16% perform 11 or more tests/month.

<table>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education-related characteristics of physicians who offer vs do not offer OFC (presented in absolute numbers and percentages)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Offers OFC n = 158</th>
<th>Does not offer OFC n = 132</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of physicians who specialized in</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergy/Immunology (%)</td>
<td>154 (97.4%)</td>
<td>127 (96.2%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Time since residency/fellowship completion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Between 1 and 5 years ago</td>
<td>42 (27.3%)</td>
<td>23 (18.0%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Between 6 and 10 years ago</td>
<td>39 (25.3%)</td>
<td>24 (18.9%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Between 11 and 19 years ago</td>
<td>37 (24.0%)</td>
<td>27 (21.3%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Between 20 and 29 years ago</td>
<td>21 (13.7%)</td>
<td>35 (27.6%)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>30 years ago or more</td>
<td>15 (9.7%)</td>
<td>18 (14.2%)</td>
<td>0.27</td>
</tr>
<tr>
<td>Number of OFCs performed during residency/fellowship</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>40 (26%)</td>
<td>66 (52%)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Up to 5</td>
<td>24 (15.6%)</td>
<td>29 (22.8%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Between 6 and 10</td>
<td>17 (11.0%)</td>
<td>5 (3.9%)</td>
<td>0.04</td>
</tr>
<tr>
<td>More than 10</td>
<td>73 (47.4%)</td>
<td>27 (21.3%)</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

OFC = oral food challenge.
As for the environment in which OFC is commonly performed, most respondents (38%) answered the hospital environment, followed by out-of-hospital/outpatient (28.5%), both (25.3%), and the rest, level III centers. Most physicians obtain informed consent from patients/guardians (89.9%). Cow’s milk (83.5%) and egg (11.4%) are the most tested foods, followed by seafood (3.2%).

Figure 3 shows the types of OFC most commonly performed (open, single-blind, or double-blind and placebo-controlled). The single-blind method is the most performed, and 74% of respondents reported only performing this method. The food is most often provided by the family (67.1%), followed by the doctor (20.3%) and nutritionist/medical staff member (12%). The food is more commonly administered to the patient by the doctor (82.3%) or a nurse/practical nurse (13.3%), and a nutritionist is only involved in 1.9% of cases.
A hundred and fifty-two physicians (45.5%) reported not offering OFC due to the following barriers: lack of appropriate resources and space (46%), lack of technical capacity (21%), inadequate reimbursement (12%), lack of health insurance (11%), and patient or family refusal (2%). Among suggested solutions (1 possible answer in the multiple-choice test), the availability of standardized national protocols for performing OFC was selected as the best one (Figure 4).

Discussion

Brazil is estimated to have a rate of 0.94 allergists/immunologists per 100,000 inhabitants under the age of 18 – more than Canada (0.67) and Australia (0.87) but much less than Germany (6.50) and Japan (3.34).

Data from this survey were obtained from all Brazilian states, except Roraima (Figure 1). The questionnaire was answered only by a small number of ASBAI members (11.6%) who voluntarily agreed...
to participate in the survey. Most respondents (n = 158/290, 54%), reported offering OFC.

The rate of respondents was low but close to that observed in a similar US survey (10%). However, 95% of respondents in the US survey reported offering OFC. A similar survey conducted in Canada obtained a response rate of 30.2%, and 80.6% of respondents reported offering OFC. In our Brazilian survey, a little over half of respondents reported offering the test, although most of them work in teaching hospitals (n = 62/158, 39%). This suggests that, despite a selection bias in favor of offering the test, OFC training is not a part of medical education in many teaching hospitals, meaning that misdiagnosis may be common. Of note, it is likely that those who do not offer this type of intervention tend to not participate in this type of survey.

Specialists who completed their residency/fellowship between 20 and 29 years ago offer less OFC in current clinical practice, probably because during their education the prevalence of FA was lower and medical residency programs did not provide OFC training. Although the rate of FA has significantly increased worldwide in the last 30 years and in Brazil in the past 2 decades, we still cannot quantify the real problem at the national level due to the scarcity of prevalence studies. No statistically significant difference was observed in those who completed their residency/fellowship > 30 years ago, probably due to the small number of respondents that constituted this group.

The performance of ≥ 5 OFCs during medical education was associated with OFC performance in current practice, showing the importance of including the procedure in medical education. More than a third (106/290) of respondents said they did not perform OFC during their residency/fellowship, higher than the rate of 29% observed in the US survey. Almost all of the allergists/immunologists who perform OFC work in more than one sector, including the private sector (148/158), and very few work exclusively in SUS (4/158) (Figure 2), meaning that most of the Brazilian population is likely to not have access to this test. Most physicians who offer OFC live in the Federal District and the Southeast Region of Brazil, possibly as a result of higher medical density in these regions, or selection bias. It was recently estimated that 63.1% of ASBAI's members live in the Southeast Region of Brazil, followed by the Northeast (15.0%), South (9.7%), Midwest (7.7%), and North (4.4%) regions.

A Canadian study reported a median of 12 OFCs per month per physician. In our survey, 62% of physicians performed up to 5 OFCs per month, and 16% performed ≥ 11 OFCs per month.

The most tested foods are cow’s milk and egg, followed by seafood, peanuts, and chestnuts. As in other countries, the open challenge is the most offered, supposedly because it is less complex. It should be noted that the rate of Brazilian physicians who obtain informed consent was similar to that of US physicians (89.9% vs. 82%) but higher than that of Canadians (40%). Although the food to be tested is often provided by family members, the doctor is the one to administer it to the patient, similarly to what happens in the USA, where the food is administered by a nurse in 73% of cases.

Unlike in the US and Canadian surveys, inadequate reimbursement was not mentioned among the main barriers by those who do not offer the test, but rather lack of appropriate resources and space (46%) and lack of technical capacity (21%). However, in Canada, dedicated reimbursement fee codes were suggested by 66.1% of respondents. Lack of support staff and office space was identified as a limitation by 72.6% and 64.5% of Canadian respondents, respectively.

Conclusion

Only a little over 50% of respondents reported offering OFC in the setting of FA, which is concerning, as the absence of testing may lead to misdiagnosis and generate unnecessary diet restrictions with nutritional risks for patients. Furthermore, we suggest that OFC should be included in medical education and complemented by refresher courses.

After the incorporation of OFC in the SUS and private health insurances, together with the increase in FA prevalence in Brazil, we expect that the demand for OFC will increase similarly to that observed in other studies. Only a little over half of the allergists/immunologists who participated in this survey claimed to offer OFC. However, we cannot rule out selection bias, as it is likely that those who do not perform OFC have chosen not to participate in this survey, which means that the frequency of OFC may be overestimated.

This study showed that access to this important diagnostic tool is very limited in Brazil, which is concerning for a country of continental dimensions.
The technical training of more professionals, either by including OFC training in residency/fellowship programs or by promoting refresher courses, is necessary. The lack of appropriate resources and spaces is also a concern that hinders the implementation and dissemination of the OFC.

Despite the selection bias inherent to the methodology used in this study, this pioneering Brazilian survey is important to understand and discuss the performance of this type of procedure in Brazil.

References


No conflicts of interest declared concerning the publication of this article.

Corresponding author:
Lucila Camargo-Lopes-de-Oliveira
E-mail: lucila_camargo@yahoo.com
Annex 1
On-line questionnaire on performing oral food challenge (OFC) aimed at specialists in allergy/immunology

Oral food challenge: Brazilian panorama

The oral food challenge (OFC) is still considered the diagnostic gold standard for food allergies (FAs) and is also used to investigate the acquisition of tolerance in patients with a previous diagnosis of FA. However, the test is not easy to perform, and it is different from food reintroduction at home. We developed this short questionnaire (approximate duration: 7 minutes) to better understand the barriers to OFC performance by ASBAI members, and we count on your valuable contribution!

ASBAI’S Scientific Department of Food Allergy (2021-2022)

Education

Did you undergo residency/fellowship training in Allergy and Immunology?
- Yes
- No

How long ago did you complete your residency/fellowship training in Allergy and Immunology?
- Between 1 and 5 years
- Between 6 and 10 years
- Between 11 and 19 years
- Between 20 and 29 years
- 30 years ago or more
- I did not undergo residency/fellowship training in Allergy and Immunology

How many OFCs did you perform during the entire period of your residency/fellowship program?
- Up to 5
- Between 6 and 10
- More than 10

In which Brazilian state (or the Federal District) do you currently work? You may select more than one option.
- Acre
- Alagoas
- Amapá
- Amazonas
- Bahia
- Ceará
- Federal District
- Espírito Santo
- Goiás
- Maranhão
- Mato Grosso
- Mato Grosso do Sul
- Minas Gerais
- Pará
- Paraíba
- Paraná
- Pernambuco
- Piauí
- Rio de Janeiro
- Rio Grande do Norte
- Rio Grande do Sul
- Rondônia
- Roraima
- Santa Catarina
- São Paulo
- Sergipe
- Tocantins
Annex 1 (continuation)
On-line questionnaire on performing oral food challenge (OFC) aimed at specialists in allergy/immunology

### Have you taken any of the following courses? You may select more than one option.
- Advanced Life Support in Anaphylaxis and Asthma (ALSAA)
- Advanced Cardiovascular Life Support (ACLS)
- Pediatric Advanced Life Support (PALS)
- None of the above

### Do you offer OFC in your clinical practice?
- Yes
- No

#### For those who offer OFC in clinical practice

### In which sector do you work as an allergist/immunologist? You may select more than one option.
- Public
- Private
- Teaching hospital (both private and public)

### What age group do you treat?
- Children and adolescents
- Adults and older adults
- All age groups

### In the last 12 months, how many patients with suspected FA did you treat on average?
- Up to 5 patients
- Between 6 and 10 patients
- Eleven patients or more

### In the last 12 months, how many OFCs did you perform per month on average?
- Up to 5
- Between 6 and 10
- Eleven or more

### In what percentage of patients with suspected FA do you perform OFC?
- Up to 25%
- 25% to 50%
- More than 50%

**When choosing the appropriate environment for performing OFC, you take into consideration:**
- The mechanism involved in the reaction (IgE-mediated or non-IgE-mediated)
- Severity of reaction
- Both

### In which environment do you typically perform OFC?
- Hospital environment
- Out-of-hospital/outpatient environment
- Both

### Do you recommend food reintroduction at home for patients with a diagnosis of non-IgE-mediated FA and for those with a history of immediate reaction without sensitization?
- Yes
- No

### If yes, has a patient ever had a severe reaction during reintroduction at home?
- Yes
- No
- I do not recommend food reintroduction at home for non-IgE-mediated cases nor for those with a history of immediate reaction without sensitization
Annex 1 (continuation)
On-line questionnaire on performing oral food challenge (OFC) aimed at specialists in allergy/immunology

Do you obtain informed consent from patients/guardians?
- Yes
- No

Which food is more commonly tested in your clinical practice?
- Cow’s milk
- Egg
- Soy
- Wheat
- Fish
- Seafood
- Peanuts and chestnuts
- Other

What type of OFC do you offer in your clinical practice? You may select more than one option.
- Open (patient, family, and doctor know which food is being administered)
- Single-blind (2-stage procedure with the food and a placebo; only the doctor knows which food is being administered)
- Double-blind and placebo-controlled (2-stage procedure with the food and a placebo, but not even the doctor knows which food is being administered)

Who provides the food that will be administered to the patient?
- Patient’s family
- You (doctor)
- Nutritionist or a medical staff member
- Other

Who typically administers the food to the patient?
- You (doctor)
- Nutritionist
- Nurse/practical nurse
- Other

For those who do NOT offer OFC

What would you describe as the main barrier to performing OFC?
- Risk of adverse effects
- Lack of technical capacity
- Lack of appropriate resources and space
- Patient or family refusal
- Inadequate reimbursement
- Lack of private health insurance

Among the options below, what would you say is the best solution to overcome these barriers?
- Well-defined criteria for when to perform OFC in a medical office or hospital environment
- Standardized national protocols for performing OFC
- Adequate reimbursement by health insurances
- In-service OFC training during residency/fellowship training
- Periodic practical courses on OFC provided by the society of which I am a member
- Hospital support close to my office to guarantee OFC safety
- Creation of reference centers for OFC in my city

Please feel free to write further considerations on the topic below.

____________________________________________________
____________________________________________________

Thank you for your valuable contribution!