



Do cross-food allergies to propofol exist?

Carles Espinós Ramírez^{1,2}, Marta Viñas Domingo¹, Anna Peig Font^{1,2},
Paula Gil Esteller^{1,2}, Maria José Castillo Marchuet¹,
Maria Pilar Saura Foix¹, Juan Carlos Martín Sanchez²,
and Maria Martínez García^{1,2}

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¹Department of Anesthesiology, Consorci Sanitari de Terrassa, Terrassa, ²International University of Catalonia, Barcelona, Spain

Corresponding author

Carles Espinós Ramírez, M.D.
Department of Anesthesiology,
Consorci Sanitari de Terrassa,
Terrassa 08036, Spain
Tel: 34-937310007
Fax: 34-937310959
E-mail: md071683@uic.es

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Background: Propofol is a short and rapidly acting intravenous anesthetic extensively used for the induction and maintenance of general anesthesia. It is a lipid emulsion that contains soybean oil, purified egg phosphatide, and egg lecithin. Therefore, the package leaflet indicates that its administration is contraindicated in patients allergic to soy, eggs, or peanuts. Our study aimed to determine whether patients with proven food allergies are allergic to propofol.

Methods: Patients of all ages allergic to soy, eggs, or peanuts who agreed to undergo skin testing for propofol allergies were included. The subjects first underwent a skin test to confirm food allergies. If candidates were negative, they were excluded. If the result was positive, a propofol skin test was performed.

Results: Sixty-four patients with confirmed food allergies underwent a propofol skin test. Only one was positive in the propofol skin test (1.6%). The patient was allergic to peanuts and soybeans. These results reinforce the idea that there is no justification for avoiding propofol use in these subjects.

Conclusions: Propofol can be safely administered to patients allergic to soy, eggs, or peanuts. We recommend caution in patients with a history of anaphylaxis after ingestion of the above-mentioned foods.

Keywords: Egg; Food allergy; Food sensitization; Peanuts; Propofol; Soy.

INTRODUCTION

Propofol is a short and rapidly acting intravenous anesthetic derived from alkylphenol (2,6-di-isopropylphenol) that is extensively used for the induction and maintenance of general anesthesia in patients older than 3 years. It is also the most widely used hypnotic among all processes that require sedation [1]. Propofol is poorly soluble in water. Its formulation consists of a lipid emulsion containing soybean and phosphatidic oils, purified egg phosphatide, and egg lecithin [2–4].

Therefore, the package leaflet indicates that its administration is contraindicated in patients allergic to soy, eggs, or peanuts.

The possible cross-reaction with peanuts is due to the existence of homologous proteins between this nut and soybeans [5]. It is known that the egg components most likely to cause allergic reactions are ovalbumin, ovomucoid, and conalbumin, which are found in egg yolk. Nonetheless, the egg component of propofol is lecithin, a highly purified phospholipid found in egg whites. Likewise, the soybean oil from

which propofol is prepared is highly refined, eliminating proteins related to allergic reactions. In fact, the remaining proteins are theoretically too small to induce an allergic reaction [2,6-8].

Some cases of allergic reactions to propofol have been published in which patients were not known to have food allergies [9-12]. There are also some publications with suspected reactions to propofol in subjects allergic to egg, soy, or peanut [13-18]. However, many of these studies have limitations. Some of them did not check with any diagnostic technique whether the patients were allergic to propofol or to foods to which cross-reactions were linked. This factor is essential because many drugs are capable of causing an allergic reaction during anesthetic induction and maintenance. It should be noted that the agents that most frequently provoke type I or immunoglobulin (Ig)-E-mediated allergic reactions are muscle blockers and antibiotics, both usually used during the perioperative period or anesthetic induction [14].

Given this controversy, our study aimed to determine whether patients with proven food allergies to soy, egg, and peanuts are also allergic to propofol. Thus, we will determine whether there is a real correlation between allergies to these foods and propofol.

MATERIAL AND METHODS

This descriptive study evaluated the prevalence of positive and negative results in a skin test for propofol allergy patients allergic to soy, eggs, and peanuts. This study was approved by the ethics committee of the Consorci Sanitari de Terrassa hospital (no. 02-20-270-056). The study was conducted at the same hospital from July 2020 to June 2021. Written informed consent was obtained from all the patients, and the study was conducted per the principles of the Declaration of Helsinki.

Study population

Patients of all ages allergic to soy, eggs, or peanuts who agreed to undergo skin testing for propofol allergies were included. They were detected in the anesthesia or allergology outpatient clinic. The participants were informed of the objectives of the study and the test they were to undergo on the same day or later by telephone. Patients were rescheduled for another day to first undergo skin testing for food allergies to eggs, peanuts, and soy. If the result was negative, candi-

dates were excluded. If the result was positive, the propofol skin test was performed.

Allergy study

Standardized skin tests, including the prick test followed by intradermal testing (0.02-0.05 ml of drug concentration) [19], were performed in all included patients. It was performed at least 4-6 weeks after any hypersensitivity reaction to minimize false negatives [20].

Skin tests were performed on eggs, peanuts, and soy. If food allergy was confirmed, a propofol skin test was performed. All tests were performed on the forearm using disposable lancets. A drop of each extract was applied to the skin, separated by at least 2 cm from the next drop.

The reading was taken 10 min after the prick test and 15 min after the intradermal tests. Positive results were defined as a papule diameter at least 3 mm greater than the negative control (saline). Histamine (10 mg/ml) was used as the positive control.

Statistical analysis

Qualitative variables are described as frequencies and percentages. Quantitative variables were described as means and standard deviations after checking their normality, and the minimum and maximum values were also reported. For the prevalence of propofol-positive tests and, due to their low presence, confidence intervals were calculated based on a binomial distribution, and proportions were compared using Fisher's test.

All intervals were calculated with a 95% confidence level, and tests were considered significant at P values < 0.05. All analyses were performed using R statistical software.

RESULTS

A total of 88 patients were recruited for this study. Nineteen patients were excluded because they did not undergo a skin test. Another five patients were excluded after refusing to undergo the propofol skin test. Finally, 64 patients with confirmed food allergies who underwent a propofol skin test were recruited. The mean age was 37 years (range: 7-78), half of whom were under 40 years old, with a female predominance (64%).

Regarding the food allergy profile, some participants were allergic to more than one food item. Sensitization to peanuts

was confirmed in 54 (84%) patients. Moreover, eight participants were allergic to eggs (13%), and nine were allergic to soy (16%). Of these, only one was positive for the propofol skin allergy test, corresponding to 1.6% of the study population (0.0–9.7%). The patient was a 25-year-old female allergic to both peanuts and soy.

See [Table 1](#) for the demographic and food allergy profiles of the participants in detail.

DISCUSSION

The debate about whether propofol should be administered to patients allergic to eggs, soy, or peanuts is still active in many countries. The present study aimed to reinforce the idea that there is no justification for avoiding propofol use in these subjects. Evaluating the results we obtained, only in one patient allergic to soy and peanuts, but not to eggs, we obtained a positive result in the skin test for propofol. Moreover, after interviewing the participant again, she was currently consuming soy without any symptoms or allergic reactions. The patient avoided consuming peanuts, although she had no clear allergic reaction. A peanut allergy was confirmed through a positive provocation test. Although she refused to consent to a propofol provocation test, we considered the result of the propofol skin test to be a true positive.

As mentioned above, the egg and soybean oil components of propofol are highly purified and refined. The size of the remaining proteins is so small that it cannot produce an allergic reaction [2,6–8]. In addition, although allergies to these foods are highly prevalent in childhood, they tend to cease during adolescence, except for peanuts.

Table 1. Demographic and Allergy Results of the Study Participant

Variable	Value (n = 64)
Demographics	
Sex	
Male	23 (37)
Female	41 (63)
Age (yr)	
< 40	32 (50)
> 40	32 (50)
Food allergies to egg, soy, or peanut	
Egg	8 (13)
Soy	10 (14)
Peanut	54 (84)
Allergic to propofol	1 (1.6)

Values are presented as number (%) or mean (95% confidence interval).

Several studies have been published that support the theory that the probability of an allergic reaction to propofol in patients allergic to the aforementioned foods is the same as in the rest of the population. Molina-Infante et al. [21] performed a retrospective study in which they evaluated 60 patients with eosinophilic esophagitis who underwent 404 endoscopies using propofol as a sedative. Up to 86% of the study population had food sensitization to soy, egg, or peanut; however, no allergic reaction was observed during the procedure.

Another retrospective study conducted in Australia [22] was focused on 28 egg-allergic children who underwent up to 43 sedations with propofol. Only one allergic reaction with clinical urticaria and generalized erythema was noted in a child with a previous history of anaphylactic reaction to egg ingestion. It was concluded that the administration of propofol in patients with suspected cross-food allergies was generally safe. Asserhøj et al. [6] conducted two retrospective studies. First, 273 patients with perioperative allergic reactions were recruited for the study. Of these, 153 were exposed to propofol, but only four had a positive allergic test for propofol. None explained the clinical reactions to eggs, soy, or peanuts. Moreover, none of them had detectable specific Ig-E levels in the blood for related foods. The second study focused on 99 patients with specific Ig-E to soy, egg, or peanut who had undergone some intervention in which propofol was administered. No allergic or associated clinical reactions were observed.

Currently, the guidelines of some countries such as France, Great Britain, and Ireland [20,22] suggest a lack of evidence for not administering propofol in patients allergic to soy, eggs, or peanuts. The Catalan Allergy Society and the Drug Allergy Committee state that there is no scientific evidence for the use of alternative anesthetic drugs in patients allergic to eggs, soy, or peanuts [23]. Other groups, such as the Childhood Allergy Committee of the Spanish Society of Allergology and Clinical Immunology, recommend avoiding propofol in egg-allergic children with a history of anaphylaxis after ingestion [3]. However, most hospitals in Spain continue to recommend avoiding the use of propofol in patients allergic to soy, eggs, or peanuts.

The relevance of our findings was strengthened by the representation of all ages in the study population. In addition, we performed a skin test to determine whether the patients were allergic to eggs, peanuts, and soy. However, our study had some limitations. Because of the coronavirus disease 2019 pandemic, we experienced greater participant loss

than expected. Therefore, the study population was smaller than expected. Thus, we cannot conclude with complete certainty that there is no risk that these patients will not present any allergic reaction to propofol administration. Although our study is one of the few prospective observational studies published in the literature, it is a descriptive study. A comparative study should be conducted to confirm that there are no differences in the incidence of propofol allergy between patients allergic to the foods mentioned here and the rest of the population. As the incidence of propofol allergy is low, a case-control study is advisable.

In conclusion, propofol could be safely administered to patients allergic to soy, eggs, or peanuts. We recommend caution or avoidance of propofol in patients with histories of anaphylaxis after ingesting the aforementioned foods.

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None.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author, CER. The data are not publicly available due to containing private patient information.

AUTHOR CONTRIBUTIONS

Conceptualization: Carles Espinós Ramírez, Marta Viñas Domingo, Maria Martinez García. Data curation: Carles Espinós Ramírez, Anna Peig Font, Maria José Castillo Marchuet, Maria Pilar Saura Foix, Juan Carlos Martín Sanchez. Formal analysis: Juan Carlos Martín Sanchez. Methodology: Carles Espinós Ramírez, Marta Viñas Domingo, Paula Gil Esteller, Maria José Castillo Marchuet, Maria Pilar Saura Foix, Maria Martinez García. Writing - review & editing: Carles Espinós Ramírez, Anna Peig Font, Paula Gil Esteller, Maria Martinez García. Investigation: Carles Espinós Ramírez. Supervision: Carles Espinós Ramírez, Paula Gil Esteller, Maria Martinez García.

ORCID

Carles Espinós Ramírez, <https://orcid.org/0000-0003-3177-5709>
 Marta Viñas Domingo, <https://orcid.org/0000-0001-7401-4630>
 Anna Peig Font, <https://orcid.org/0000-0003-4338-5206>
 Paula Gil Esteller, <https://orcid.org/0000-0003-2807-4784>
 Maria José Castillo Marchuet,
<https://orcid.org/0000-0002-1938-2403>
 Maria Pilar Saura Foix, <https://orcid.org/0000-0001-7888-5302>
 Juan Carlos Martín Sanchez,
<https://orcid.org/0000-0002-1045-4802>
 Maria Martínez García, <https://orcid.org/0000-0001-5622-5346>

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