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Propofol use in pediatric patients with food allergy and eosinophilic esophagitis

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Abstract

Propofol is a safe, well-tolerated anesthetic that is labeled as contraindicated in patients with egg or soy allergy. This contraindication has become increasingly problematic given the rising incidence of food allergy and eosinophilic esophagitis (EoE). To address this issue, we studied practice patterns of propofol use for esophagogastroduodenoscopies (EGD) in children with EoE and food allergies at our institution. A retrospective observational study of 1365 EGDs from January 2013 to June 2014 was performed. Data was analyzed using student t-tests, chi square tests, Fisher's exact tests, and multivariable logistic regression. We found that propofol was used significantly less in patients with egg or soy allergy, as well as in patients with EoE, even after adjusting for the presence of food allergy. There was no difference in complication rates relative to propofol use. Propofol was used safely in pediatric patients with EoE and food allergy in this limited single-center review.

Keywords

soy allergy; egg allergy; anesthesia

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Introduction

Propofol (2,6-diisopropylphenol) is commonly used as an anesthetic agent during pediatric esophagogastroduodenoscopy (EGD) (1). Since propofol contains egg phospholipids and soybean oil, it is contraindicated in patients with egg or soy allergy (2). Although egg phospholipids and soybean oils are not thought to be allergenic (3, 4), there remains a theoretical risk of cross contamination with egg or soy protein and case reports implicate propofol as the inciting trigger for IgE-mediated reactions in some patients with egg or soy allergy (5-7). In contrast, some studies and clinical practice, suggest that propofol is safe to use in patients with these allergies (8, 9). This issue has become even more relevant given an increasing incidence of eosinophilic esophagitis (EoE), a disease characterized by food allergies and the need for frequent endoscopies.

Because of this clinical conundrum, we studied the practice patterns with respect to propofol use in children with EoE and food allergies at our institution. We performed a retrospective analysis determining the rate of propofol use and associated complications in children undergoing EGD with a clinical history of egg or soy allergy or EoE.

Methods

Screening of EPIC medical records of all children ages 0 through 18 years who underwent general anesthesia for EGD at Children's Hospital Colorado (CHCO) from January 1, 2013 to June 30, 2014 was used to identify patients. Patients were excluded from analyses if procedures other than pH impedance were simultaneously performed with the EGD. Comorbidities and allergies were determined by reviewing the patient's problem list and were included if listed prior to the EGD date. Personal and familial anesthetic histories were obtained from the anesthesiologist's pre-operative notes. Complications were determined by reading all post-operative notes completed within one week of the procedures. This study was approved by the Colorado Multi Institutional Review Board (COMIRB) with a waiver of informed consent.

Data was analyzed using a Student t-test for continuous variables and Pearson chi-square test and Fisher's exact test for categorical variables. Multivariable logistic regression was used to determine the odds of using propofol after adjusting for age, gender, comorbidities, and presence of egg or soy allergy. Because 6% of patients had more than one EGD, additional sensitivity analysis was performed. A generalized estimation equation was used to account for the clustering effect of repeated EGDs on the same patient. Multivariable logistic regression was also performed after excluding data from repeated measures of multiple EGDs. Statistical analysis was carried out using SAS software package 9.4 (SAS Institute, Inc., Cary, NC).

Results

Characteristics of the patient population

Chart review of the medical records of 1,365 EGDs performed on 1,279 patients was completed (see Table 1). General anesthesia was used for all procedures and was performed by 48 anesthesiologists. Fifteen procedures were performed on 12 patients with a history of anaphylaxis to egg; propofol was used in 6 of these. One patient had 3 procedures – the first two without propofol and the third with propofol. One procedure was performed on a patient with a history of anaphylaxis to soy and propofol was not given. No significant differences were identified in American Society of Anesthesiologists (ASA) classifications between patients who received propofol and those who did not ($p=0.88$).

Propofol use in food allergic and EoE patients

Propofol was used significantly more in patients without egg or soy allergy than those with allergy (72% versus 40%, $p < 0.0001$). Propofol was used significantly less in patients with EoE than those without EoE (55% versus 71%, $p < 0.0001$). Propofol was used significantly more in older children (11 versus 7 years, $p < 0.001$) and in females (71% versus 65%, $p=0.02$). After adjusting for possible confounders including the presence of egg or soy allergy, gender, age, and asthma, patients without EoE were still significantly more likely to receive propofol than those with EoE ($p = 0.04$). In the adjusted analysis, patients without EoE were 40% more likely to receive propofol than those with EoE (OR 1.4, 95% CI [1.02, 1.92]). The adjusted odds ratios are depicted in Figure 1.

Complication rates

Procedural complications are described in Table 2. No hospital admissions or anaphylactic episodes were identified in any patient. There was no significant difference in total complication rates between patients who received propofol and those who did not regardless of allergic or EoE diagnoses. One respiratory complication was recorded in a non-EoE, egg / soy allergic child who received propofol. This 3-year-old girl had a history of recent upper respiratory infection and developed postoperative laryngeal irritability. She required positive pressure ventilation and albuterol nebulization, was treated with cool mist oxygen and discharged home on room air.

Discussion

Pediatric patients with EoE frequently require sedated endoscopies for management of their disease. Propofol is an anesthetic agent commonly used during endoscopy; however it is contraindicated in patients with egg or soy allergy. Because EoE is associated with food allergy, propofol use in this patient population is controversial. Therefore, we performed a retrospective review of EGDs in pediatric patients over a 1.5-year period in our tertiary care children's hospital. We found that patients with egg or soy allergy were less likely to receive propofol. Patients with EoE were also less likely to receive propofol even after adjusting for the presence or absence of egg or soy allergy. Finally, there was no difference in rate of anesthetic complications in patients who received propofol relative to those who did not,

irrespective of their diagnosis of EoE or food allergy. In this series, propofol was safely administered to pediatric patients with EoE and food allergy.

Our study showed that nearly half of all EGDs on soy or egg allergic patients were performed with propofol. Thus, despite its contraindication, propofol is commonly used for pediatric patients with egg or soy allergy at our institution. This practice is consistent with other studies documenting that propofol is commonly used in these patients despite the warning. Based on the fact that no significant adverse events were found in 149 procedures performed on 131 children with soy, egg or nut allergies, Wiskin et al reported that propofol is the sole anesthetic agent used for pediatric EGDs in their institution (10). They were careful to report that this group included those with IgE and non-IgE mediated allergies.

In our study, even after adjusting for egg or soy allergy, propofol was used less frequently in patients with EoE. The reasons for this are unclear; however, we hypothesize that it might be due to concerns about the potential for unidentified soy or egg allergy in a patient population with a disease process that is often food allergen driven. Despite the prevalence of egg and soy allergy among patients with EoE, only 1 study has examined propofol use in this population. Molina-Infante et al performed a retrospective chart review of 60 adult EoE patients sensitized to egg, soy, or peanut who received propofol. Similar to our findings, they did not identify anaphylactic reactions or severe adverse reactions in EoE patients with egg and soy allergy and concluded that propofol could safely be administered to egg or soy allergic patients (11).

Some studies suggest that patients may have physical responses to propofol that are not IgE mediated. For instance, patients may have allergic responses that are due to chemical properties of propofol rather than cross contamination with egg or soy. Laxenaire et al described a series of 14 patients who developed anaphylaxis to propofol and who later had confirmatory testing supporting hypersensitivity to propofol's phenyl or isopropyl group rather than egg. Several of these patients later had skin prick or intradermal testing to intralipid (a product that also contains egg lecithin and soybean oil) and were all found to be skin test negative (12). In a larger adult study, Asserhoj et al systematically investigated propofol allergy in patients with suspected perioperative allergic reactions by using serum tryptase, specific IgE levels, skin-prick testing, intradermal testing, and IV propofol provocation tests. The authors found that 2.6% of these patients had positive allergy tests and none had allergic symptoms when eating egg or soy (13). Finally, some patients may have non-IgE mediated reactions to egg or soy that are yet to be well defined.

As the incidence of both pediatric food allergy and EoE continues to rise, the number of endoscopies performed on these patient populations will likely grow as well. Given propofol's warning, questions regarding the safety of propofol administration in this highly atopic group will likely persist. Propofol has been commonly used as an anesthetic for decades; however, the contraindication for its use in patients with egg or soy allergy began in 2007 (2, 14). The anesthetic properties of propofol were first described in 1973 with subsequent European clinical trials in the mid-1970s (15, 16). The original formulation contained Cremophor EL, a castor oil related substance, but was withdrawn due to a high rate of anaphylaxis (16-19). It was then reformulated using its current lipid-based emulsion

in the mid-1980s and entered the US market in 1989 (16). Despite the new formulation, several reports of anaphylaxis persisted through the next decade (5, 6, 20-22). In 2007, the FDA issued an alert and revised the label to include a propofol infusion syndrome warning (2, 23) as well as egg and soy allergy contraindication to use.

Studies seeking to fully assess the safety of propofol in egg and soy allergic children are not feasible to complete given the rarity of propofol allergy and the large numbers of patients needed to definitively answer this question. Since the incidence of allergic reaction to propofol is 1:10,000 to 1:20,000 and the incidence of propofol anaphylaxis is 1:60,000, a much larger sample size is needed to address the safety profile of propofol in the allergic population (24, 25). We felt it was important to perform this retrospective study in spite of this issue because of our interest in EoE, the number of EGDs that these patients undergo, and the common presence of both IgE and non-IgE mediated food allergies.

Our study has several limitations. While propofol is an increasingly common choice for anesthesia, many factors other than EoE or allergies can influence its use. The diagnosis of food allergy was based on review of the medical record. Thus, whether these patients had IgE or non-IgE-mediated food allergy is uncertain and could not be further characterized. Because physicians make medical decisions based on both parental report and medical records, this study is reflective of real-life practices. Patients undergoing endoscopy may or may not have allergy testing results in their medical records. Additionally, positive allergy tests may be indicative of sensitization rather than true allergy. Though this study provides support that propofol is safe in patients with reported egg and soy allergy, the study cannot make a definitive statement regarding overall safety.

Results from our retrospective study of a limited number of patients found that propofol was used safely in children with EoE and in those with egg/soy allergy. Even after accounting for food allergy, it was used less frequently in EoE patients. Further work is needed to better define food allergic diseases, understand potential mechanisms of propofol related reactions and determine optimal care of EoE patients who have IgE and/or non-IgE-mediated egg and soy allergies.

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What is known

- Propofol is commonly used for pediatric anesthesia given its safety and favorable side effect profile.
- Because it is formulated with an egg and soy based lipid solvent, propofol use is controversial in children with food allergy.

What is new

- Propofol is frequently used in egg or soy allergic patients despite a contraindication warning on the package insert.
- Patients with EoE are less likely to receive propofol even after accounting for egg or soy allergy.
- Propofol was used safely for EGDs in pediatric patients with EoE or food allergy in this single-center review.

Figure 1.

Adjusted odds ratios for using propofol after controlling for presence of age, sex, egg/soy allergy, asthma, and eosinophilic esophagitis (EoE). The odds of using propofol for esophagogastroduodenoscopies performed on patients without egg or soy allergy are 2.5 times greater than those performed on patients with food allergy. Procedures performed on patients without EoE are 40% more likely to be performed with propofol even after adjusting for presence of egg or soy allergy.

Table 1

Characteristics of the patient population

	Egg or soy allergy (no EoE)	No egg or soy allergy (no EoE)	EoE only (no egg or soy allergy)	EoE and egg or soy allergy
Age (years)	6.9	9.7	9.7	6.8
Gender				
Male (%)	42 (58)	477 (46)	112 (68)	63 (69)
Female (%)	31 (42)	559 (54)	53 (32)	28 (31)
Number of patients	68	1005	130	76
Number of procedures	73	1036	165	91
Number of procedures using propofol (%)	38 (52)	747 (72)	114 (69)	27 (30)

Table 2

Procedural complications stratified by patient type

EGG/SOY ALLERGIC PATIENTS			
COMPLICATION	Number of procedures		P-value
	No propofol (N =98)	Propofol given (N =64)	
Nausea and Vomiting	2	1	1.00
Respiratory Difficulties	1	1	1.00
Unanticipated Admission	0	0	---
Anaphylaxis	0	0	---

EOE PATIENTS			
COMPLICATION	Number of procedures		P-value
	No propofol (N =115)	Propofol given (N = 141)	
Nausea and Vomiting	8	6	0.34
Respiratory Difficulties	0	0	---
Unanticipated Admission	0	0	---
Anaphylaxis	0	0	---

NON-ALLERGIC, NON-EOE PATIENTS			
COMPLICATION	Number of procedures		P-value
	No propofol (N =323)	Propofol given (N = 783)	
Nausea and Vomiting	14	33	0.93
Respiratory Difficulties	4	11	0.83
Unanticipated Admission	0	0	---
Anaphylaxis	0	0	---