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Propofol Administration in Patients with an Egg Allergy

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PROPOFOL ADMINISTRATION IN PATIENTS WITH AN EGG ALLERGY

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Abstract

Title: Propofol Administration in Patients with an Egg Allergy

Background: Propofol, commonly marketed as Diprivan, is a frequently administered intravenous medication used by anesthesia providers for induction of anesthesia, maintenance of anesthesia, or moderate to deep sedation. There has been a long-standing debate in the healthcare community about whether propofol can be administered to patients with an egg allergy. Conflicting statements and inconclusive evidence have resulted in confusion among clinicians.

Purpose: The purpose of this literature search is to provide an extensive review of the literature regarding propofol administration in patients with an egg allergy. A universal, evidence-based, consensus should be determined regarding if propofol can be used safely in patients with an egg allergy.

Process: A literature review was conducted using the Cochrane Library, PubMed, CINAHL, and SCOPUS databases which were accessed through the University of North Dakota's Harley E. French Library of the Health Sciences. Other pertinent literature was found by searching the reference lists of initially acquired articles. All literature was evaluated extensively and applied to this paper or rejected due to substandard information.

Results: A review of the literature revealed case reports of anaphylactic or anaphylactoid reactions that occurred after the administration of propofol in adult patients, but egg allergies were not a causative factor in these reports. Although it has been confirmed that propofol can cause life-threatening, anaphylactic reactions, studies have shown that it is unrelated to egg allergies in adult patients. The literature regarding propofol administration in pediatric patients with egg allergies is vague and nonconfirmatory. Studies state that it is probably safe to

administer propofol to pediatric patients with egg allergies unless they have had an anaphylactic reaction to eggs.

Implications: Anesthesia providers may be unnecessarily choosing an anesthetic agent with an inferior safety profile in place of propofol administration in patients with an egg allergy.

Keywords: Propofol, egg allergy, anaphylaxis, allergic reaction, and allergy management

Propofol Administration in Patients with an Egg Allergy

Propofol, commonly marketed as Diprivan, is a frequently administered intravenous medication used by anesthesia professionals. It is most often used for induction of anesthesia, maintenance of anesthesia, or moderate to deep sedation. Propofol is a popular drug among anesthesia providers due to its quick onset and ultra-short acting effects (Nagelhout & Plaus, 2014). There has been a long-standing debate about whether propofol can be administered to patients with an egg allergy. Propofol warning labels in some countries list hypersensitivities to eggs as a contraindication to its use (Dewhirst, Naguib, & Tobias, 2011). However, these warning labels vary from country to country regarding the administration of the drug in patients with egg allergies (Asserhoj, Mosbech, Kroigaard, & Garvey, 2015). The warning labels vary between countries even when the same formulation of the drug is used (Murphy, Campbell, Baines, & Mehr, 2011). There have been many case reports written about anaphylactic reactions to propofol, but the mechanism of action remains unclear. The case reports are lacking confirmatory evidence linking propofol administration in patients with an egg allergy to an adverse reaction. Conflicting statements and inconclusive evidence have resulted in confusion among clinicians (Asserhoj et al., 2016).

Propofol is an important drug used in anesthesia practice due to its rapid onset and emergence. Propofol is also a popular choice over other induction agents because it decreases post-operative nausea and vomiting, decreases pruritus, and exhibits anticonvulsant properties. It is often regarded as a relatively safe drug, but common adverse effects include mild to moderate hypotension, transient respiratory depression or apnea, and mild to moderate pain on injection (Flood, Rathmell, & Schafer, 2015). Some anesthesia providers refrain from administering

propofol in patients allergic to eggs even though there is no definitive evidence confirming this is a true contraindication (Dewhirst et al., 2011).

A universal evidence-based consensus needs to be determined on whether propofol can be used in patients with egg allergies. A case report of a patient with an egg allergy who received propofol will be recounted and a literature review of this topic will be discussed in the following pages.

Purpose

The purpose of this independent project is to present a case report of an adult patient with an egg allergy who safely received propofol with induction and to present literature confirming it can be safely used in this patient population. This is significant because anesthesia providers may be avoiding propofol in situations where it might be the best option because they are concerned about a possible allergic reaction.

Case Report

A 29-year-old, 22 kilogram (kg), 119 cm, male presented for surgical wound closure. Past medical history included anorchidism, moderate-persistent asthma, bronchopulmonary dysplasia, chromosomal abnormality, congenital lobular emphysema, proportional dwarfism, hypospadias, mild mental retardation, multiple congenital facial anomalies, and nephrolithiasis. Past surgical history included tracheostomy, gastrostomy, external auditory canal reconstruction, orchiopexy, hernia repair, right testicle removal, gastric fundoplication, and dental surgery. Current medications included mometasone furoate, cholecalciferol, budesonide, ipratropium-albuterol, benefiber, epinephrine as needed (PRN), carbamide peroxide 6.5% PRN, docusate sodium PRN, and guaifenesin PRN. The patient had an extensive list of allergies which included milk protein, latex, sulfamethoxazole/trimethoprim, egg white, egg yolk, erythromycin, and

rocephin. The allergy to milk protein was known to cause anaphylaxis, the latex allergy was known to cause dyspnea, and the rocephin allergy was known to cause hives. The patient was given an American Society of Anesthesiologists (ASA) physical status class of III.

An airway assessment of this patient revealed a Mallampati class II, a thyromental distance of fewer than three fingerbreadths, mouth opening of greater than three fingerbreadths, limited neck range of motion, a receding chin, and a small, disproportionate head. The patient had a previous tracheostomy site that was no longer used, but still appeared to be moderately patent. This site was utilized for endotracheal tube placement during a recent dental procedure. Preoperative vital signs included blood pressure 120/67 mmHg, heart rate 86/min, respiratory rate 20/min, temperature 36.4 degrees Celsius, and oxygen saturation (SpO2) of 96% on room air. His physical assessment revealed a regular heart rate and rhythm and bilateral clear lung sounds auscultated throughout.

After the pre-operative assessment had been completed, the patient was deemed as having an anticipated difficult airway. A glidescope was brought into the operating suite proactively. The anesthesia care team decided that Plan A would be to insert an endotracheal tube (ETT) through the prior tracheostomy site, as was done during a procedure at an outside facility a few weeks prior. Plan B was to insert a laryngeal mask airway (LMA) for the procedure.

The patient was transported to the operating room (OR) and assisted on to the operating room table per OR staff. Standard monitors were applied which included a blood pressure cuff, 5-lead EKG, and pulse oximetry. The patient was calm and pleasant. An inhalation induction was performed with 5L of nitrous oxide, 3 L of oxygen, and varying concentrations of Sevoflurane. A twenty-gauge, intravenous (IV) peripheral catheter was inserted in the left

forearm after the patient was anesthetized. After IV placement, the patient was given fentanyl 50 micrograms (mcg) IV and propofol 50 milligrams (mg) IV. Intubation through the tracheostomy site with an ETT was attempted, but unsuccessful due to strong resistance with advancement. A size 2.5 LMA was successfully inserted and gauze was placed over the tracheostomy site. Confirmation of a patent airway was confirmed by bilateral breath sounds, positive end-tidal CO2 (ETCO2), and symmetrical chest rise. A nasopharyngeal temperature probe was inserted into the left nare for precise temperature monitoring and continuous ETCO2 monitoring was utilized. Vancomycin 350 mg IV was infused over sixty minutes prior to surgical incision. Propofol 20 mg IV and fentanyl 25 mcg IV were given shortly after incision due to symptoms of pain and agitation. Normal Saline 500 ml IV was infused and the patient required phenylephrine 125 mcg IV, given in incremental doses, throughout the case. Adequate ventilation was maintained throughout the intraoperative period. Decadron 4 mg IV and Zofran 3 mg IV were given prior to emergence to prevent nausea and vomiting. The patient was extubated awake with no issues and transferred to the post-anesthesia recovery unit (PACU). The patient's time in the PACU was uneventful and he did not require any additional medications. He did not exhibit any signs of an allergic reaction throughout his perioperative experience and was discharged home from phase II without incident.

Literature Search

Formulating a PICO question for this literature search helped to clearly state what literature needed to be reviewed. PICO questions are designed to show the elements of an issue in a clear and structured way so that a literature review of the question can be done effectively. PICO stands for population (P), intervention (I), comparison (C), and outcome (O). A well-designed PICO question will decrease time spent on and increase the efficiency of a literature

review (Stillwell, Fineout-Overholt, Melnyk, & Williamson, 2010). The following PICO question was developed to articulate the components of the issue of propofol administration in patients with egg allergies. Among surgical patients with an egg allergy (P), does administration of propofol (I/C), result in allergic reactions perioperatively (O)?

Databases

Stillwell et al. (2010) recommends beginning a search to answer a research question by using the Cochrane Library, PubMed, and CINAHL databases. The Cochrane Library is considered to have the greatest level of evidence due to the excellent study designs used in their articles. The Cochrane Library, PubMed, CINAHL, and SCOPUS databases were accessed from the Harley E. French Library of the Health Sciences for this literature review. These databases were employed because they contain medical, scientific, and nursing literature (Stillwell et al., 2010).

Vocabulary and Limits

The terms propofol and egg allergy were typed under "title, abstract, keywords" on the Cochrane database and one relevant article was found. Alternatively, a search of propofol allergy was initiated and the box to limit the results to the last ten years was checked. This resulted in eighteen articles, three of which were relevant to this topic.

The search completed in the PubMed database was accomplished using MeSH terms to utilize its controlled vocabulary thesaurus. Using MeSH terms makes a search all-encompassing by finding all articles related to the concept. Typing in propofol and allergy also pulled up the MeSH terms hypersensitivity and immunology. This search resulted in one hundred thirty-one results. To make the number of articles more approachable the limits "full text," "within ten years," "humans," and "free full text" were applied which decreased the search results to sixteen.

Within the CINAHL database, the CINAHL headings option was utilized for a more effective search. CINAHL headings are similar to MeSH terms in PubMed. At first, the term propofol was used and the box to limit it to a major concept was checked. This resulted in one thousand three hundred fifty-six articles. Instead, the terms propofol and allergy were entered which resulted in five pertinent articles.

The SCOPUS database was utilized by typing in propofol and allergy under "article title, abstract, keywords" and applying the limits "articles," "English," "human," and "2012-2016". This resulted in forty-nine articles. Another search in SCOPUS was completed by typing in propofol under "article title" and adding a field to include egg allergy under "article title, abstract, keywords". This search resulted in six articles.

Additional Search Means

In addition, a search was completed using the Chester Fritz Library website as it extracts articles from several databases. One applicable article was found by reading an editorial with an additional relevant article cited within. Two more significant articles were discovered by reading through the reference list of one of the high-quality research articles that had already been evaluated. The use of controlled vocabulary within credible and healthcare specific databases proved to be efficacious in this literature review.

Review of Literature

To evaluate the research on propofol administration in patients with an egg allergy effectively, it is best first to know and understand the pathophysiology of allergic reactions and specifically egg allergies. The literature on these topics will be discussed first followed by a discussion regarding the administration of propofol in adults and children with a documented egg

allergy. Lastly, treatment of patients who exhibit an allergic or anaphylactic reaction will be covered.

Allergic Reactions

An anaphylactic reaction refers to a severe, life-threatening, rapidly developing, type I hypersensitivity. Anaphylactic reactions occur due to an antigen-antibody interaction in a patient who has been exposed to the antigen in the past and has become sensitized. These reactions are IgE-mediated, which means IgE antibodies found on mast cells and basophils react with an antigen which causes the release of mediators. It is the mediators that cause the symptoms of an allergic reaction which may include anaphylaxis (Lee et al., 2012; Nagelhout & Plaus, 2014). It has been estimated that the incidence of anaphylaxis during anesthesia is rare, occurring in one in ten thousand cases (Koul, Jain, & Sood, 2011). Symptoms of anaphylaxis are systemic, occur rapidly, and may include "pruritus, urticaria, angioedema (especially laryngeal edema), hypotension, wheezing and bronchospasm, and direct cardiac effects, including arrhythmias" (Nagelhout & Plaus, 2014, p. 1023). Anaphylactoid reactions also cause a mediator release, but are not triggered by an IgE-mediated reaction. Symptoms of these types of reactions may be similar in presentation to an anaphylactic reaction, but are typically less severe (Nagelhout & Plaus, 2014). Anaphylaxis during anesthesia is a rare occurrence, and thus, the diagnosis of the problem can often be delayed (Lee et al., 2012).

In anesthesia, many drugs have been implicated in causing anaphylactic and anaphylactoid reactions. Neuromuscular blocking agents top the list of medications that cause anaphylactic reactions with an estimated fifty to seventy percent of all reported cases (You et al., 2012). Neuromuscular blocking agents are followed by latex and then antibiotics in order of most commonly causing anaphylaxis (Lee et al., 2012; Nagelhout & Plaus, 2014). According to

Lee et al. (2012) “hypnotics, opioids, local anesthetics, colloids, aprotinin, and protamine were found to be less frequently involved” (p. 827) in allergic reactions. Anaphylactic reactions to propofol administration have been infrequently reported, but the cause of the reactions have not been inconclusively determined (Harper, 2016).

Egg Allergies

Eggs are one of the most common causes of food allergies in children and the mechanism has been most often linked to an IgE-mediated, type I hypersensitivity reaction, although non-IgE-mediated reactions have also been reported. Allergic conditions such as atopic dermatitis and eosinophilic esophagitis have also been seen with eggs (Caubet & Wang, 2011; Martorell et al., 2013). Children with an egg allergy usually exhibit symptoms before the age of two, which typically reflects the first dietary exposure to the food product. An estimated fifty percent of children reach tolerance by four years of age and sixty-six to seventy-four percent reach tolerance by five years of age. Up to ninety percent of reactions to eggs affect the skin, followed by the gastrointestinal system, and less frequently the respiratory system. Egg allergy occurrence is greater in children who have a cow’s milk allergy and in those with atopic dermatitis (Caubet & Wang, 2011; Martorell et al., 2013). Interestingly, the patient in this case report had an allergy to eggs and an allergy to milk.

There are five allergenic proteins that have been identified in eggs and four of them are found in egg white. The four allergic components found in egg white include ovomucoid, ovalbumin, ovotransferrin, and lysozyme. Ovalbumin is the most profuse protein found in egg white, but ovomucoid is the leading allergen. IgE-mediated ovomucoid allergy is also credited to children who have a more persistent egg allergy compared to those who outgrow their allergy to egg (Caubet & Wang, 2011). According to Martorell et al. (2013) both the egg white and egg

yolk can cause allergic sensitization, but only the egg white has been found to cause an allergic response. Only two of the nine proteins found in egg yolks are thought to be allergenic which does not include lecithin, the component utilized in propofol (Murphy et al., 2011). The major allergen found in egg yolk is alpha-livetin, or chicken serum albumin, and this is not found in propofol (Dewachter, Mouton-Faivre, Castells, & Hepner, 2011).

An important detail regarding egg allergies is that most children outgrow them, so reevaluations should be completed throughout life (Caubet & Wang, 2011). The patient in this case report had many listed allergies, but information was not provided on when these allergies were first reported and if testing was done for these allergies after childhood.

Propofol and Allergies

According to Harper (2016) in 1994 a single case of pruritus following the administration of propofol to a patient with an egg allergy lead to the consideration of avoiding propofol in egg allergic patients, thus beginning the whole debate. Propofol is a lipid emulsion formulation and an alkylphenol derivative (2,6-di-isopropyl-phenol) that contains 100 mg/ml of soybean oil, 12 mg/ml of egg lecithin, sodium hydroxide, phosphatides, and glycerol (Dewachter et al., 2011; Kelso, 2014; Martorell et al., 2013). It should be noted that propofol was specifically designed with allergic reactions in mind (Dewhirst, Naguib, & Tobias, 2011). The egg lecithin, a highly-purified phosphatide, which can be found in propofol comes from egg yolk, but egg white contains the most allergy containing proteins (Molina-Infante et al., 2014). Propofol has two possible components that can cause an allergic reaction, a phenol group and a di-isopropyl side chain. Reactions to propofol, although rare, are often credited to the di-isopropyl group if reported on the first exposure and due to the phenol molecule if reported after repeated exposure to the drug (Inal, Memis, Vatan, Cakir, & Yildiz, 2008; Koul et al., 2011).

Many case reports of anaphylaxis to propofol administration have been described, but most of them have been attributed to the phenol group or di-isopropyl side chain rather than an egg allergy. Inal et al. (2008) and Koul et al. (2011) describe two different case reports of patients who had an anaphylactic reaction, confirmed by post-operative allergy testing, to propofol. The patients had no prior allergies listed in their medical records. Symptoms after receiving propofol varied and included a full-body rash, severe hypotension, pulmonary edema, and oedema. In one of the cases the patient also had a skin test completed on the ten percent intralipid portion of propofol, but it was negative. The authors in both case reports concluded that there are two potential allergic components of propofol, the di-isopropyl side chain and the phenol molecule (Inal et al., 2008; Koul et al., 2011).

Allchurch and Crilly (2014) describe a case report of a patient who had a fixed drug eruption, or the appearance of multiple cutaneous skin lesions, following the administration of propofol. This patient also had no known allergies. The authors of this case report concluded that the exact pathophysiology of this reaction could not be explained (Allchurch & Crilly, 2014).

A randomized controlled trial was completed to determine the safety of using propofol in patients with allergic diseases and/or bronchial asthma. They found that the incidence of wheezing and bronchoconstriction after propofol administration was higher in this patient population than in patients without allergic disease or bronchial asthma. Interestingly, all patients with egg allergies were excluded from this study, yet severe reactions still occurred (Nishiyama, 2013). This indicated that although propofol has been implicated as causing allergic reactions, allergies to eggs has not shown to be the causative factor.

Tashkandi (2010) stated in a case report that patients with egg allergies are allergic to the egg protein or albumin, not the lecithin which is present in propofol. It was also suggested that

allergic reactions after the administration of propofol are more likely in patients with atopy, because “it can cause a nonimmunologic, nonspecific histamine release” (p. 208). However, Kimura, Adachi, and Kubo, (1999) describe a prospective randomized controlled study done on patients with “any history of allergy such as bronchial asthma, atopic dermatitis, allergic rhinitis, food-induced allergy, drug-induced allergy, hay fever, contact-type dermatitis, and cold urticaria” (p. 582) in which only one patient in the study exhibited a high degree of histamine release after propofol administration. Furthermore, propofol was shown to produce the same amount of histamine release as seen with a Versed-Ketamine combination given for induction. Interestingly, the process of placing an endotracheal tube itself was shown to cause histamine release in twelve of the patients. No adverse reaction to propofol was observed during this study, but the authors still concluded that propofol should be used carefully in patients with a history of allergic diseases (Kimura et al., 1999).

It is important to note that in all the case reports described thus far none of the patients had allergies to eggs. However, there were still anaphylactic or anaphylactoid reactions following propofol administration. This indicates there are other causative factors, other than egg allergy, which need to be considered.

Propofol and Egg Allergies

In this extensive literature review several high-quality research articles were found that determined propofol can be safely used in adult patients with an egg allergy. Pongdee (n.d.) concluded that although there are trace amounts of residual proteins contained in egg lecithin, no allergic reaction has been shown to be caused by egg lecithin and patients with egg allergies can receive propofol without any special precautions.

A retrospective study was completed on two cohorts to ascertain if the current practice of avoiding propofol in patients with egg, soy, or peanut allergies is evidence-based. Study A included patients who had a peri-operative allergic reaction during 2004-2011 and were exposed to propofol, while Study B included patients greater or equal to sixteen years of age who had an IgE-mediated egg, soy, or peanut allergy. Study A completed allergy testing on the patient population, while Study B utilized questionnaires and chart reviews to collect data through 2004-2012. In study A only four of the one hundred fifty-three patients had positive allergy tests to propofol and only one of these patients showed a possible IgE-mediated allergic reaction to propofol, evidenced by a positive skin test and elevated serum tryptase. Importantly, none of these four patients stated they had an egg, soy, or peanut allergy and they all had negative specific IgE tests completed on egg or soy. Study B found that the ninety-nine patients who had IgE-mediated egg, soy, or peanut allergies had no allergic reaction when given propofol. The authors of these studies concluded that the avoidance of propofol in patients allergic to egg, soy, and peanuts is not evidence-based and propofol can be given safely to this patient population (Asserhoj, Mosbech, Kroigaard, & Garvey, 2016).

A retrospective observational study was conducted to assess the safety of propofol administration in patients with both eosinophilic esophagitis (EoE) and an egg, soy, legume, or peanut allergy. Eighteen of the patients in this study, fourteen to fifty-six years of age, had an eggs, soy, or peanut allergy, while fifty-two of the patients had a sensitization to one of these foods. Atopy was present in eighty-eight percent of the study participants. No allergic reaction was reported in any of the endoscopies, except one episode of a bronchospasm in a fourteen-year-old boy with asthma. The bronchospasm occurred after intubation, the patient received multiple drugs for general anesthesia, and an allergic work-up was negative for all drugs given

during the procedure. Notably, some of the patients in this study received propofol for the first time while the others had received propofol multiple times before. The patients who had received propofol multiple times account for possible IgE-mediated allergic reactions. This study found that propofol can be safely administered to patients with an egg, soy, or peanut allergy and warning labels on propofol should be reconsidered (Molina-Infante et al., 2014). Molina-Infante et al. (2014) states that:

> The US Food and Drug Administration does not contraindicate the administration of Intralipid® in egg- or soy-allergic patients. Therefore, it makes no sense to contraindicate propofol in these patients considering that propofol and Intralipid® share the same egg and soy content. (p.391)

Fisher (2007) describes a study conducted over a twenty-eight-year span of one hundred forty-four patients who were referred to an allergy clinic. The referral was aimed at patients who had a presumed risk of anaphylaxis to anesthetic drugs due to their medical history or family history. Intradermal skin testing for allergies was performed on drugs such as propofol, midazolam, and neuromuscular blockers. Two of the patients had an egg allergy history, but had negative skin tests to propofol. Furthermore, they both had received propofol multiple times in the past with no signs of an allergic reaction (Fisher, 2007).

Pediatric Population

The review of literature regarding the use of propofol in pediatric patients with an egg allergy was less straightforward than what was found in a review of the adult population. IgE-mediated egg allergies most commonly occur in the pediatric population. Seventy-five percent of children who are allergic to eggs tolerate egg yolk without incidence. Additionally, the amount of egg yolk protein in egg lecithin is minimal and is highly unlikely to produce an allergic

reaction (Murphy et al., 2011). A retrospective analysis was done on children, aged one to seventeen years, to determine if propofol administration in patients with either non-IgE or IgE-mediated allergies to eggs, soy, or nuts is safe. Although thirteen undesirable events occurred, with the majority being respiratory in nature, none of them were accredited to propofol. One allergic reaction occurred, but was due to the first appearance of an unknown latex allergy. The authors of this study concluded that it is most likely safe to administer propofol to children with egg or soy allergies and that this is in agreement with the limited published information available on this topic with respect to the pediatric population (Wiskin, Smith, Wan, Nally, & Shah, 2015).

A retrospective case review regarding the safety of propofol administration was completed on a sample of children, aged one to fifteen years, with IgE-mediated allergies to egg or soy. Forty-two out of forty-three patients received propofol with no issue, including one child with a severe history of egg anaphylaxis. Another child with a history of IgE-mediated allergies to eggs (with a prior anaphylactic reaction), milk, nuts, and sesame developed a nonanaphylactic reaction after receiving propofol for the first time. Symptoms included generalized erythema and urticaria, and he was subsequently treated with adrenaline, IV hydrocortisone, and oral trimeprazine. A skin prick test for propofol was positive, but testing for ten percent Intralipid was not completed. It was undetermined if the reaction was due to residual egg allergens or the isopropyl/phenol components of propofol. A conclusion was made that propofol can be safely administered in most pediatric patients with egg allergies. However, the study only included two children with a history of egg anaphylaxis, one who reacted to propofol and one who did not. Therefore, it was deduced that propofol should be avoided in children with a history of egg anaphylaxis until further research is completed on this specific population (Murphy et al, 2011). Harper (2016) agreed that although propofol appears safe to administer to children with a

moderate egg allergy, it should be avoided in children who have had a past anaphylactic reaction to egg until more research can state indisputably otherwise.

Treatment of Anaphylaxis

If an anaphylactic reaction to propofol, or any other medication/material, occurs treatment and post-evaluation should be completed. The main risk factor for anaphylaxis to drugs is a previous uninvestigated, immediate reaction. If a prior immediate hypersensitivity reaction or undiagnosed adverse reaction during anesthesia has been noted in a patient's medical record, allergy assessment and testing should be completed prior to elective surgical procedures. If a suspected allergic reaction transpires the provider should carefully note the symptoms that occur and refer the patient for allergy testing once stable (Fisher, 2007; Dewachter et al., 2011).

Recognition of anaphylaxis during anesthesia can be delayed and the initial diagnosis of anaphylaxis may need to be presumptive due to its life-threatening nature. Treatment of anaphylaxis begins with maintaining a patent airway and administering 100% oxygen. Epinephrine should be utilized as soon as anaphylaxis is suspected since its alpha-1 properties correct hypotension while its beta-2 properties relax bronchial smooth muscle (Nagelhout & Plaus, 2014). A single dose of epinephrine is usually enough to treat most incidences of anaphylaxis (Koul et al., 2011). However, the dose and frequency of epinephrine administration depends on the severity of the symptoms. Intravenous fluids should be largely utilized to compensate for the peripheral vasodilation that occurs during anaphylaxis. Antihistamines may be utilized during anaphylaxis to treat urticaria and angioedema. H1-receptor antagonists with or without H2-receptor antagonists may also be used to combat refractory hypotension. Glucocorticoids may be given to prevent a prolonged reaction or a biphasic anaphylactic reaction. A biphasic anaphylactic reaction occurs when symptoms resolve and then reoccur

many hours later (Lee et al., 2011; Nagelhout & Plaus, 2014). A serum tryptase level should be drawn about one hour after a reaction because it indicates mast cell activation and can be a helpful gauge of anaphylaxis (Dewachter et al., 2011). Martorell et al. (2013) describes a monoclonal antibody, omalizumab, that binds to and forms macrocomplexes with circulating IgE. This complex effectively prevents the immunoglobulin from binding to its receptors on "mast cells, basophils, dendritic cells, and lymphocytes" (p.328) It is currently used for the treatment of asthma, but clinical trials are still evaluating its utilization in patients with food allergies (Martorell et al., 2013; Nagelhout & Plaus, 2014).

Discussion

The patient described in this independent project had an extensive list of allergies including milk protein, latex, sulfamethoxazole/trimethoprim, egg white, egg yolk, erythromycin, and rocephin. The most interesting aspect of his allergy list is that he was specifically allergic to both egg white and egg yolk, yet he did not have an allergic reaction when given propofol. The patient exhibited moderate hypotension following the induction. However, hypotension is a common side effect of propofol and fentanyl, which were both administered to the patient. However, he did not exhibit any other signs of a possible allergic reaction such as pruritus, urticaria, angioedema, wheezing, bronchospasm, or arrhythmia.

As discussed in the literature, individuals with egg allergies are allergic to egg whites, but the egg lecithin found in propofol is derived from the egg yolk. The egg lecithin is still thought to be very unlikely to cause an allergic reaction in patients with an egg yolk allergy because it is highly refined and contains minimal egg yolk protein. The case report described in this independent project coincides with the current research that states patients with an egg allergy can safely be given propofol.

Conclusion

Propofol continues to list egg allergy as a contraindication to its use on warning labels. However, these labels vary by country and multiple studies have shown that this is not a true contraindication. More consistency among labeling should be achieved, especially with new research showing quite the opposite of this contraindication.

Although it is certain that propofol can cause an anaphylactic or anaphylactoid reaction, the cause of these reactions is inconclusive, but decidedly unrelated to egg allergies in the adult population. Although research also shows that children with moderate egg allergies can be safely given propofol, more research needs to be done before conclusions can be undoubtedly made on the use of propofol in the pediatric patient with a prior anaphylactic reaction to eggs.

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PROPOFOL ADMINISTRATION IN PATIENTS WITH AN EGG ALLERGY

Katie King, SRNA

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Introduction

- There has been a long-standing debate about whether propofol can be administered to patients with an egg allergy. Propofol warning labels in some countries list hypersensitivities to eggs as a contraindication to its use
- However, labels vary from country to country even when the same formulation is used
- Conflicting statements and inconclusive evidence has resulted in confusion among clinicians

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Introduction

- There have been many case reports written about anaphylactic reactions to propofol, but the mechanism of action remains unclear.
- The case reports lack confirmatory evidence linking propofol administration in patients with an egg allergy to an adverse reaction.

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Case Information

- Wound Closure
- 29-year-old
- 22 Kilograms
- 119 centimeters
- Male
- ASA III

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Pre-operative Evaluation

- Past Medical History
  - anorchidism, moderate-persistent asthma, bronchopulmonary dysplasia, chromosomal abnormality, congenital lobular emphysema, proportional dwarfism, hypospadias, mild mental retardation, multiple congenital facial anomalies, and nephrolithiasis
- Surgical History
  - Tracheostomy, gastrostomy, external auditory canal reconstruction, orchiopexy, hernia repair, right testicle removal, gastric fundoplication, and dental surgery

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Pre-operative Evaluation

- Allergies
  - Milk protein, latex, egg white, egg yolk, erythromycin, rocephin, and sulfamethoxazole/trimethoprim
- Current Medications
  - Mometasone furoate, cholecalciferol, budesonide, ipratropium-albuterol, benefiber, epinephrine as needed (PRN), carbamide peroxide 6.5% PRN, docusate sodium PRN, and guaifenesin PRN

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Pre-operative Evaluation

- Airway evaluation
  - Mallampati class II, a thyromental distance of fewer than three fingerbreadths, mouth opening of greater than three fingerbreadths, limited neck range of motion, a receding chin, and a small, disproportionate head
  - Previous nonpatent tracheostomy site

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Pre-operative Evaluation

- Pre-op Vital Signs
  - Blood pressure 120/67 mmHg
  - Heart rate 86/min
  - Respiratory rate 20/min
  - Temperature 36.4 degrees Celsius
  - Oxygen saturation (SpO2) of 96% on room
- Regular heart rate and rhythm; bilateral clear lung sounds

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Anesthetic Course

- Drugs
  - ***Propofol 90 mg IV given in divided doses***
  - Fentanyl 75 mcg IV given in divided doses
  - Decadron 4 mg IV
  - Zofran 3 mg IV
  - Phenylephrine 125 mcg IV given in divided doses
  - Vancomycin 350 mg IV

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Anesthetic Course

- Technique
  - Size 2.5 LMA inserted
    - Successful placement and adequate ventilation throughout short procedure
    - Gauze placed over tracheostomy site

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Intraoperative Issues/PACU

- Intraoperative Issues
  - Hypotension
    - Treated with a total of 500 ml of LR and 125 mcg IV Phenylephrine
- PACU
  - Time in the PACU was uneventful
  - No signs of an allergic reaction throughout his perioperative experience
  - Discharged home from phase II without incident

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Propofol Administration in Patients with an Egg Allergy:

Review of Literature

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Discussion

- To evaluate the research on propofol administration in patients with an egg allergy effectively, it is best first to know and understand the pathophysiology of allergic reactions and specifically egg allergies.
- The literature on these topics will be discussed first followed by a discussion regarding the administration of propofol in adults and children with a documented egg allergy.

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Anaphylactic/Anaphylactoid Reaction

- An anaphylactic reaction refers to a severe, life-threatening, rapidly developing, type I hypersensitivity (occurs rarely in anesthesia)
- Occurs due to an antigen-antibody interaction in a patient exposed to the antigen in the past and has become sensitized.
- Reactions are IgE-mediated
  - IgE antibodies found on mast cells and basophils react with an antigen causing the release of mediators

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Anaphylaxtic/Anaphylaxtoid Reaction

- The release of mediators cause the symptoms of an allergic reaction which may include anaphylaxis
- Symptoms are systemic and occur rapidly
  - Pruitus, uricaria, angioedema, laryngeal edema, hypotension, wheezing, bronchospasm, arrhythmias
- Anaphylactoid reactions may also cause mediator release, but are not triggered by an IgE-mediated reaction and symptoms are usually less severe

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Anaphylaxtic/Anaphylaxtoid Reaction

- Neuromuscular blocking agents top the list of medications that cause anaphylactic reactions (~50-70% of all reported cases)
- This is followed by latex and antibiotics
- Hypnotics, opioids, local anesthestics, colloids, aprotinin, and protamine were found to be less commonly involved
- Anaphylactic reactions to propofol administration have been infrequently reported and the cause undetermined

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Egg Allergies

- Eggs are one of the most common causes of food allergies in children and the mechanism has been most often linked to an IgE-mediated, type I hypersensitivity reaction
- Usually exhibited before 2 years old (first dietary exposure)
- ~50% reach tolerance by 4 years old
- ~66-74% reach tolerance by 5 years old

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Egg Allergies

- Up to 90% of reactions to eggs affect the skin, followed by the GI system, and less frequently the respiratory system
- Egg allergy occurrence is greater in children with a cow's milk allergy and in those with atopic dermatitis

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Egg Allergies

- Ovomucoid, found in egg white, is the leading allergen and is found in children with persistent egg allergy
- Only two of the nine proteins found in egg yolks are thought to be allergenic
  - Does not include lecithin which is utilized in propofol.

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Egg Allergies

- Major allergen in egg yolk is alpha-livetin, or chicken serum albumin, and this is not found in propofol
- Both the egg white and egg yolk can cause an allergic sensitization, but only the egg white has been found to cause an allergic response

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Propofol and Allergies

- Propofol is a lipid emulsion formulation and an alkylphenol derivative (2,6-di-isopropyl-phenol) that contains 100 mg/ml of soybean oil, 12 mg/ml of egg lecithin, sodium hydroxide, phosphatides, and glycerol
- Specifically designed with allergies in mind
- The egg lecithin, a highly purified phosphatide, found in propofol comes from egg yolk, but egg white contains the most allergy containing proteins

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Propofol and Allergies

- Propofol has two possible components that can cause an allergic reaction, a phenol group and a di-isopropyl side chain
  - Case reports of anaphylaxis to propofol have been described, but most of them have been attributed to the di-isopropyl side chain (on first exposure) or the phenol group (after repeated exposure) rather than an egg allergy

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Propofol and Allergies

- Two different case reports were described of patients who had an anaphylactic reaction, confirmed by post-operative allergy testing, to propofol. The patients had no prior allergies listed in their medical records. The authors in both case reports concluded that there are two potential allergic components of propofol, the di-isopropyl side chain and the phenol molecule (Inal et al., 2008; Koul et al., 2011)

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Propofol and Allergies

- A randomized controlled trial was completed to determine the safety of using propofol in patients with allergic diseases and/or bronchial asthma. They found that the incidence of wheezing and bronchoconstriction after propofol administration was higher in this patient population than in patients without allergic disease or bronchial asthma. All patients with egg allergies were excluded from this study, yet severe reactions still occurred (Nishiyama, 2013).

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Propofol and Allergies

- Allchurch and Crilly (2014) describe a case report of a patient who had multiple cutaneous skin lesions, following propofol administration although he had no known allergies to egg.
- In all the case reports that were reviewed in which patients had an anaphylactic/anaphylactoid reaction to propofol, none of the patients had allergies to egg

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Propofol and Egg Allergies

- A retrospective study was completed on two cohorts to determine if the practice of avoiding propofol in patients with egg, soy, or peanut allergies is evidence-based.
- The first cohort included patients who had a peri-operative allergic reaction and were exposed to propofol and the second included patients who had an IgE-mediated egg, soy, or peanut allergy.
- In the first cohort 4 out of 153 patients had positive allergy tests to propofol. Only 1 of these 4 patients showed a possible IgE-mediated allergic reaction to propofol.
- None of these 4 patients stated they had an egg, soy, or peanut allergy and they all had negative specific IgE tests completed on egg or soy. 99 patients in the second cohort who had IgE-mediated egg, soy, or peanut allergies had no allergic reaction when given propofol.
- This study concluded that propofol can be safely administered in patients allergic to egg, soy, and peanuts.

(Asserhoj, Mosbech, Kroigaard, & Garvey, 2016) UND Nurse Anesthesia University of North Dakota

Propofol and Egg Allergies

- A retrospective observational study was conducted to assess the safety of propofol administration in patients with both eosinophilic esophagitis (EoE) and an egg, soy, legume, or peanut allergy.
- In this study 18 patients had an allergy and the other 52 patients had a sensitization to one of these foods.
- No allergic reactions were reported in any of the cases in which patients received propofol. Some of the patients in this study received propofol for the first time while the others had received propofol multiple times before (accounting for IgE-mediated allergies).

(Molina-Infante et al., 2014) UND Nurse Anesthesia University of North Dakota

Propofol and Egg Allergies

Pediatric population

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Propofol and Egg Allergies

- 75% of children who are allergic to eggs tolerate egg yolk without incidence and the amount of egg yolk in egg lecithin is highly unlikely to produce an allergic reaction.
- A study was completed to determine if propofol administration in children with either non-IgE or IgE-mediated eggs, soy, or nut allergies is safe. No undesirable events that occurred were accredited to propofol.
- One allergic reaction transpired, but was due to the first appearance of an unknown latex allergy. It was concluded that it is likely safe to administer propofol to children with egg or soy allergies

(Wiskin, Smith, Wan, Nally, & Shah, 2015) UND Nurse Anesthesia University of North Dakota

Propofol and Egg Allergies

- A retrospective case review regarding the safety of propofol administration was completed on a sample of children with IgE-mediated allergies to egg or soy. Within this sample, 42 out of 43 patients received propofol with no issue, including one child with a severe history of egg anaphylaxis.
- Another child with a history of egg anaphylaxis developed a nonanaphylactic reaction after receiving propofol for the first time. Symptoms included generalized erythema and urticaria

(Murphy, Campbell, Baines, & Mehr, 2011) UND Nurse Anesthesia University of North Dakota

Propofol and Egg Allergies

- A skin allergy test for propofol was positive, but testing for the 10% Intralipid component was not completed. Therefore, it was undetermined if the reaction was due to residual egg allergens or the isopropyl/phenol components of propofol.
- This study concluded that propofol can be safely administered in most pediatric patients with egg allergies. However, since the study only included 2 children who have had an anaphylactic reaction to eggs it was deduced that propofol should be avoided in these children until further research is completed.

(Murphy, Campbell, Baines, & Mehr, 2011)

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Recommendations

- Although it is certain that propofol can cause an anaphylactic or anaphylactoid reaction, the cause of these reactions is inconclusive, but decidedly unrelated to egg allergies in the adult population
- Although research also shows that children with moderate egg allergies can be safely given propofol, more research needs to be done before conclusions can be undoubtedly made on the use of propofol in the pediatric patient with a prior anaphylactic reaction to eggs

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Conclusion

- Most individuals with egg allergies are allergic to egg whites, but the egg lecithin found in propofol is derived from egg yolk. The egg lecithin is thought to be very unlikely to cause an allergic reaction in patients with an egg yolk allergy because it is highly refined and contains minimal egg yolk protein
- The patient described in the initial case report was allergic to both egg white and egg yolk, yet he did not have an allergic reaction when given propofol. The case report described coincides with the current research that states patients with an egg allergy can safely be given propofol.

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Thank You
Are There Any Questions?

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