Perioperative Anesthesia Considerations for Patients with Alpha Gal Syndrome

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Contents

Abstract

Background: Alpha-gal syndrome (AGS) is a lesser-known allergic syndrome that is prevalent in North Carolina and presents a significant risk to perioperative patients. Perioperative patients with AGS are at high risk for an allergic reaction as they are exposed to many potential triggering agents in a short period of time. **Purpose:** The purpose of this project is to increase anesthesia provider knowledge regarding AGS and its perioperative implications. **Methods:** This quality improvement project was conducted at a large, tertiary hospital and included a preintervention survey, educational intervention, introduction of a site-specific cognitive aid, and post-intervention evaluation. **Recommendations and Conclusion**: Surveys revealed a significant knowledge gap in anesthesia providers regarding AGS. Implementation of an educational intervention and cognitive aid was associated with a statistically significant increase in average knowledge scores for surveyed anesthesia providers. Likert scale questions reflecting AGS knowledge were numericized and averaged using Excel to reflect an interval change. AGS education is therefore recommended to further improve knowledge and ensure patient safety. Anesthesia providers should be encouraged to foster discussions with multidisciplinary teams to identify patients with AGS and avoid triggering agents for these patients. Pharmacy involvement is recommended to maintain up to date information regarding medication and surgical product safety.

Key Words

Alpha-gal syndrome; AGS; Alpha-gal allergy, mammalian meat allergy; Lone Star tick; beef allergy; red meat allergy; anesthesia; perioperative

Background and significance

Alpha-gal syndrome (AGS) is a serious and life-threatening allergic reaction to mammalian meat which occurs after a tick bite. It is relevant to anesthesia because commonly administered perioperative medications and surgical products may contain the alpha-gal epitope, and potentially elicit anaphylactic reactions. Gabapentin taken by mouth (PO) and intravenous (IV) Dilaudid are two commonly administered medications that may contain triggering ingredients (U.S. National Library of Medicine, 2020). Onset of symptoms varies depending on route of administration. Reactions to orally administered triggering agents occur 4-6 hours after exposure, while reactions to intravenously administered triggering agents can occur within minutes (Wilson et al., 2019; Young et al., 2021). Therefore, reactions may occur in any perioperative phase. The prevalence of AGS is unknown, however studies suggest that up to 20% of the population in North Carolina may have serum IgE antibodies to alpha-gal (Chung et al., 2008; Commins et al., 2011; O'Neil et al., 2007). Due to the potential severity of reactions and the likelihood that anesthesia providers in North Carolina will care for a patient with AGS, it is imperative that they be aware of the syndrome and ways to mitigate risk for their patients.

It is widely recognized that certain medications and surgical products can place AGS patients at risk of anaphylaxis in the worst-case scenarios; however, providers may lack the awareness to prevent this exposure. A 2017 study in North Carolina found that out of 100 medical encounters, correct diagnosis or effective referral happened in less than 10% of patients later discovered to have AGS (Flaherty et al.). This demonstrates a gap in provider awareness to consider AGS as a potential cause of anaphylaxis. In patients presenting with idiopathic

anaphylaxis, 9% were found to have AGS and experienced no further episodes of anaphylaxis with avoidance of red meat consumption (Carter et al., 2018).

Purpose

The aim of this project was to increase anesthesia provider knowledge of an allergic syndrome that has emerged over the last two decades and the threat it poses to perioperative patients, especially in North Carolina. Through an educational in-service and implementation of a potential AGS trigger medication list, this project sought to improve anesthesia provider knowledge and increase patient safety. The educational intervention addressed common signs and symptoms of AGS, potential allergens and advocated for increased awareness in perioperative staff, specifically in addressing what medications are safe for administration to this population. In treating patients with AGS, the primary goal should be avoiding exposure to potential triggering agents (D'Ercole et al., 2019. Dunkman et al., 2019). A site-specific potential AGS trigger medication list was implemented, detailing the risks or safety for AGS patients of commonly administered medications in the perioperative period.

Review of Current Evidence

Search Strategy

Pubmed, CINAHL and Cochran library were utilized to conduct a literature review with the search terms "alpha-gal", "meat allergy", "periop*", "anesthes*", "tick", "Lone Star", and "medication". The topic of interest was an overview of AGS and its relation to medications commonly administered in the anesthesia setting. All research study designs within a five-year date range were included. Landmark articles, although older than five years were also included.

Only articles in the English language were included. References from selected studies were evaluated for relevance and utilized if specific to Alpha-Gal syndrome. Thirty-two articles were identified and included. Main themes covered: AGS prevalence and distribution, typical signs and symptoms, timing of onset of symptoms, potential drug reactions, and anesthetic/perioperative risks in patients with AGS.

Alpha-Gal Syndrome

Alpha-gal syndrome (AGS), otherwise known as mammalian meat allergy or red meat allergy is an allergy to galactose-α-1,3-galactose (alpha-gal) (Chung et al., 2008), a carbohydrate found in the meat and tissues of non-catarrhine mammals (Hilger et al., 2019). Catarrhine refers to Old World monkeys, including orangutans, gorillas, chimpanzees, and humans. Alpha-gal can be found in the meat of pigs, cows, rabbits, lamb, and venison. Poultry, seafood, reptiles, and humans do not contain alpha-gal. The syndrome was inadvertently discovered during clinical trials of the monoclonal antibody Cetuximab, in which a disproportionately higher incidence of hypersensitivity reactions was noted to occur in southeastern states (Chung et al., 2008; O'Neil et al., 2007). Chung et al.'s results assisted in the discovery of a new and serious food allergy to beef, pork, and lamb associated with IgE antibodies to alpha-gal (Chung et al., 2008; Commins et al., 2009; Jacquenet, S., 2009).

An accumulating body of research suggests tick bites cause the syndrome, but researchers have not been able to show what in ticks triggers the immunoglobulin E (IgE) response or why certain people develop AGS (Chinuki et al., 2016; Commins et al., 2011; Crispell et al., 2019; Khoury et al., 2018). In North America, A. *Americanum* or the Lone Star tick is the primary species of exposure, but other species have been linked to Alpha-gal syndrome globally (Young et al., 2021).

Provider Lack of Awareness

As with all allergies, the primary objective is the avoidance of potential triggers (Dunkman et al., 2019; Wolfe et al., 2021). Lack of provider awareness of potential triggering agents (Dunkman et al., 2019) and inability to identify patients with AGS pose a significant barrier to perioperative patient safety (Carter et al., 2018; Dunkman et al., 2019; Flaherty et al., 2017; Wolfe et al., 2021). The average time to diagnosis for patients with AGS is 7.1 years (Flaherty et al., 2017), which may reflect the lack of provider knowledge. Even when patients are diagnosed with AGS, electronic health records may not have a standardized way to reflect this allergy. Alpha-Gal allergy, beef allergy, mammalian meat allergy, and red meat allergy are synonymous with AGS and must be recognized as such or inquired about with the patient.

Identifying potential triggers is a complicated and dynamic process with serious consequences if not achieved. Recognition of anaphylaxis is particularly challenging during anesthesia as the classic signs of hypotension and bronchospasm can result from other causes during general anesthesia. Skin changes such as a rash or hives may not be immediately visible under the surgical drapes. Death, cardiac arrest, myocardial infarction, acute kidney injury, memory and coordination problems, increased hospital stays, delayed surgeries, anxiety and posttraumatic stress disorder (PTSD) have all been identified as potential outcomes of anaphylaxis (Harper et al. 2018). With such severe outcomes at risk, providers need to keep allergic reaction and anaphylaxis at the top of their minds for differential diagnosis to promptly treat reactions. Prevention of allergic reactions is the goal, however when not achieved, rapid recognition and initiation of treatment become paramount. Prompt administration of epinephrine is associated with better outcomes (Harper et al. 2018).

Prevalence of Alpha-Gal Syndrome

The true prevalence of AGS is unknown (U.S. Department of Health and Human Services (HHS), 2020). There is currently no requirement for healthcare providers to report diagnoses of AGS nor an International Classification of Disease diagnosis code to establish a baseline (HHS, 2020). The Centers for Disease Control and Prevention is working with Viracor Eurofins Clinical Diagnostics, the only company that currently tests for AGS, to update the number of cases and create a consistent reporting process (HHS, 2020). Studies suggest that up to 20% of the population in North Carolina may have serum IgE antibodies to alpha-gal (Chung et al., 2008; Commins et al., 2011; O'Neil et al., 2007).

Distribution of Alpha- Gal Syndrome

In the United States most reports of AGS are in the mid-west and eastern states (Young et al., 2021). Ecological niche models of the Lone Star tick find its distribution across the Eastern seaboard and in the Upper Midwest, but it is expected to have northward and westward expansion with climate change (Rhagavan et al., 2019). Informal data shows that as of 2019, Raleigh, NC was the third most-represented city in the two primary Facebook AGS support groups (U.S. Department of Health and Human Services (HHS), 2020). Those who reside in mid-west and eastern areas of the United States are at higher risk of incurring a tick bite from the Lone Star tick and developing AGS (Rhagavan et al., 2019). Thus, providers in these areas need to be educated on strategies for identification of AGS and be aware of potential complications.

Common signs and symptoms

AGS can be serious and life-threatening with the majority of patients reporting anaphylaxis (Young et al., 2021). The estimated incidence of perioperative anaphylaxis from all causes is 1 in

10,000 anesthetics (Harper et al. 2018). Perioperative anaphylaxis accounts for one third of anaphylaxis cases admitted to critical care (Gibbison et al., 2012). Mortality related to anaphylaxis is 3-6%, with 2% having poor neurological outcomes (Mills et al., 2013).

In a systematic review of 18 observational studies, Young et al. (2021) report that 88.9% of diagnosed AGS patients experienced skin reactions (83.3% urticaria) after exposure to alpha-gal, Anaphylaxis was reported in 77.8%, and gastrointestinal symptoms in 55.6% (Young et al., 2021). In an observational study of 261 patients, 93% reported urticaria, 60% anaphylaxis, and 64% gastrointestinal issues (Wilson et al., 2019). Severity of symptoms may vary due to amount of alpha-gal and/or titer of the patients IgE to alpha-gal (Dunkman et al., 2019).

Onset of symptoms

Oral Consumption

Most patients report onset of symptoms two to six hours following oral consumption (Wilson et al., 2019; Riess & Nourian, 2023; Young et al., 2021). However, it is important to note that symptom onset in some patients was reported to occur in as little as ten minutes following oral consumption (Young et al., 2021). A limitation to these findings is that many of the studies relied on detailed questionnaire and self-reports to measure the time of symptom onset (Wilson et al., 2019; Young et al., 2021).

Intravenous Injection

Case reports demonstrate that reactions occur sooner following administration of a known alpha-gal triggering agent via an intravenous route (Young et al., 2021). Patients who received a known AGS-triggering agent intravenously had reactions within minutes of medication administration (Chung et al., 2008; Young et al., 2021). These same patients reported delayed

reactions after orally consuming beef or pork (Chung et al., 2008), suggesting that intravenous routes of administration lead to more rapid reaction onset. Most medications used during the perioperative period are administered intravenously, thus anesthesia providers must be aware of potential triggers and vigilant to promptly recognize signs of reactions.

Treatment of AGS Reactions

Treatment of symptoms thought to be related to alpha-gal hypersensitivity is the same as treatment for general hypersensitivities which includes epinephrine, H1 and H2 antagonists, albuterol, epinephrine, and supportive measures (Dunkman et al., 2019).

Anaphylaxis is an uncommon, life-threatening systemic hypersensitivity reaction, usually due to an allergy. On average, anesthetists will encounter a patient with perioperative anaphylaxis every 7.25 years (Harper et al., 2018). Perioperative anaphylaxis is unique in that many medications are given almost concurrently. Additionally, most medications are delivered intravenously, creating the potential for rapid and severe reactions (Harper et al., 2018). Anaphylaxis during anesthesia is also unique because patients are often not alert and cannot report subjective symptoms such as pruritus, abdominal pain, nausea, and dyspnea. The clinical features noted specifically for anaphylaxis in a perioperative setting (versus anaphylaxis in other settings) are hypotension (46%), bronchospasm (18%), tachycardia (9.8%), cyanosis or oxygen desaturation (4.7%), bradycardia (3%), and reduced capnography (2.3%) (Harper et al., 2018). Cardiac arrest, hypotension and bronchospasm are the most common presenting features (Harper et al., 2018). Rash is an uncommon presenting feature, however developed eventually in 56% of cases (Harper et al., 2018).

The largest prospective study of anaphylaxis found that immediate management by anesthetists was ‘good’ in 46% and ‘poor’ in 15% of cases (Harper et al., 2018). Deficits noted in treatment were delayed cardiac compressions, insufficient fluid administration, late or omitted epinephrine administration, and delay in recognition or initiation of anaphylaxis treatment (Harper et al., 2018).

If anaphylaxis is suspected, the administration of epinephrine and fluids are the standard for immediate clinical management (Harper et al., 2018; Manian & Volcheck, 2022). Cardiopulmonary resuscitation should be initiated without delay if indicated (Harper et al., 2018; Manian & Volcheck, 2022). Vasopressin and glucagon (for patients on beta blockers) may be administered, depending on patient presentation (Harper et al., 2018; Manian & Volcheck, 2022). Corticosteroids and antihistamines may be given, however there is limited data for their effectiveness in this setting (Harper et al., 2018; Manian & Volcheck, 2022).

Perioperative Risks

Enhanced Recovery After Surgery

Since perioperative patients are exposed to a multitude of medications within a short period of time, this population is at high risk of exposure to triggering agents and the potential life-threatening anaphylaxis that may ensue. Enhanced Recovery After Surgery (ERAS) protocols are widely utilized multimodal approaches to improve patient recovery after surgery. ERAS aims to decrease opioid dependence by utilizing a combination of nonopioid medications. Gabapentin is a gabapentinoid, traditionally used for nerve pain and epilepsy, which has become a routine ERAS medication. Many oral medications contain meat byproducts used in the manufacturing of pills, capsules, and tablets. Most formulations of oral Gabapentin contain gelatin, a common

triggering agent of AGS (U.S. National Library of Medicine, 2020). ERAS protocols require caution as oral Gabapentin, Celecoxib, and others may contain byproducts suspected to be allergens, such as glycerin or magnesium stearate (D'Ercole et al., 2019; Dunkman et al., 2019).

Triggering Agents

In addition to allergic reactions to Cetuximab and mammalian meat, patients with this syndrome need to be cautious of other medications and products derived from mammals that may contain alpha-gal. Many potential allergens in medications are related to inactive compounds used in the manufacturing of the drug, such as gelatin, glycerin, magnesium stearate, lactic acid, and stearic acid (D'Ercole, 2019; Dunkman et al., 2019; Wolfe, 2021). Some of these substances can be derived from either plants or animals, which makes identifying potential triggers challenging. Manufacturers are not currently required to report or provide the source of their ingredients. Formulations of one drug may vary by manufacturer, making identification even more challenging and site-specific.

Nourian et al. describe a process for screening each vial anticipated for use in caring for a patient with AGS (2023). This process includes identifying the National Drug Code number, found on the label of each medication, and entering it into the National Institutes of Health (NIH) sponsored drug database, DailyMed (dailymed.nlm.nih.gov) (Nourian et al., 2023). The provider then scanned the medication ingredients for the potentially triggering inactive compounds previously mentioned (Nourian et al., 2023). Since this can be a time-consuming process and pharmacy will be aware of new manufacturers for medications on formulary, it is recommended that anesthesia collaborate with pharmacy to keep medication lists current (Dunkman et al., 2018, Nourian et al., 2023).

Gelatin

Alpha-gal is present in gelatin, which is manufactured from the bones and connective tissues of animals. Gelatin has been reported to cause allergic reactions in AGS patients via processed foods, vaccines, gelatin colloids, capsules, and hemostatic agents (Caponetto et al., 2013; Lied et al., 2019; Mullins et al., 2012; Stone et al., 2017; Stone et al., 2019; Vidal et al., 2016). Commonly used ERAS medications such as Gabapentin and Celecoxib often contain gelatin and can be triggering agents (U.S. National Library of Medicine, 2020). Nausea is a common side effect of anesthesia and surgery, so antiemetics are typically administered. An antiemetic, Aprepitant (brand name- Emend) often contains gelatin and should be avoided in AGS patients, unless they have been shown to tolerate oral gelatin-containing medications.

Some AGS patients may tolerate oral gelatin but have anaphylactic reactions to the intravenous administration of gelatin (Mullins et al., 2012; Uyttebroek et al., 2014). Tolerance to oral gelatin may be determined by reviewing current medications and scanning for gelatin containing drugs (Nourian et al., 2023). Many institutions now recognize gelatin as a potential allergen for those with AGS (D'Ercole, 2019; Dunkman et al., 2019; Wolfe, 2021).

A growing body of evidence connects anaphylaxis in alpha-gal patients after vaccination with vaccines containing high amounts of gelatin (Schmidle et al., 2021; Stone et al., 2017; Stone et al., 2019). Absorbable hemostatic materials, such as Surgiflo, Gelfoam and Floseal are commonly used in surgery to assist hemostasis and contain porcine and/ or bovine gelatin (Lied et al., 2019; Wolkow et al., 2018). One case report details a patient with AGS who suffered severe intraoperative anaphylaxis shortly after Surgiflo was placed over sutures (Lied et al.,

2019). Artificial gelatin colloids are other potential triggering agents for patients with AGS (Mullins et al., 2012).

Glycerin

Glycerin is a potential AGS-triggering agent because it is derived from mammals (Dunkman et al., 2019). However, no studies found in the literature review showed evidence of glycerin-provoking allergic reactions in patients with AGS. Propofol is one of the most commonly administered anesthetic drugs and is dissolved in glycerin (Nourian et al., 2023). However, Fresenius Kabi, a manufacturer of Diprivan (a brand of Propofol), currently utilizes plant-based glycerin (Nourian et al., 2023). Other manufacturers of Propofol should be contacted to determine plant or animal origins.

Lactic Acid and Stearic Acid

Both stearic and lactic acid may be derived from plant and animal sources. Those derived from animal sources may contain alpha-gal. Although no case studies were found crediting these acids with triggering AGS reactions, many sources list them as ingredients for AGS patients to avoid (D'Ercole et al., 2019; Dunkman et al., 2019). Stearic acid and lactic acid are often ingredients in oxycodone tablets and hydromorphone injections (Dunkman et al., 2019). One study cited Lactated Ringer's fluid as being a potential trigger as it contains lactic acid (Nourian et al., 2023).

Magnesium Stearate

Magnesium stearate is another ingredient used in manufacturing that can be derived from either animal or plant product, and thus potentially trigger an AGS reaction. Muglia et al. report a case study of a patient with confirmed AGS who experienced allergic symptoms of chest

tightness, laryngeal edema, abdominal cramping, nausea, diarrhea, and hives after taking a variety of medications (acetaminophen, naproxen, lisinopril, hydrocodone/acetaminophen, and clonidine) with one common inactive ingredient—magnesium stearate (2015). Since identifying magnesium stearate as the potential allergen and eliminating it, he has had no further reactions (Muglia et al., 2015).

Heparin

Unfractionated heparin (UFH) is a derivative of porcine intestinal mucosa and bovine lung, which may contain the alpha-gal epitope (Nwamara et al., 2022). UFH has been associated with a low incidence of AGS reactions (2.6%) when administered at lower doses, such as 5,000 units for venous thromboembolism (Nwamara et al., 2022). However, at higher doses for AGS patients undergoing cardiopulmonary bypass, there is a risk of up to 50% serious allergic reactions (Hawkins et al., 2020).

Some sources suggest considering a heparin desensitization strategy (McRae et al., 2022), pre-treatment with diphenhydramine and steroids (Sell-Dottin et al., 2017; Kleiman et al., 2017), or the selection of alternative anticoagulants such as Bivalrudin (Radwan et al., 2020). Due to the potential risk of variability in heparin lots, one group suggests a heparin challenge the night before a procedure and use of the same manufacturer's lot for subsequent surgical dosing (Kleiman et al., 2017).

Bioprosthetic products

In addition to medications as potential AGS triggers, conventional bioprosthetic valves have porcine or bovine origins and contain alpha-gal epitope in connective tissue (Konakci et al., 2005). These valves are treated with glutaraldehyde to decrease antigenicity, sterilize, and

improve mechanical strength (Mozzicato et al., 2014). However, glutaraldehyde-treated xenografts can still provoke an anti-alpha gal response (Bloch et al., 2011; Mozzicato et al., 2014).

Decellularized valves were previously reported to have no detectable alpha-gal (Kasimi et al., 2005), but in vitro testing confirms the presence of alpha-gal even in decellularized products (Kuravi et al., 2022). These lab findings indicate that clinically, patients with AGS may experience strong immune responses to these materials, which can lead to accelerated valve degeneration (Hawkins et al., 2021; Kuravi et al., 2022) and coronary artery disease (Kuravi et al., 2022).

Conceptual Framework/Theoretical Model

Lewin's theory of change was used in the implementation of this project. The first step is unfreezing—letting go of old concepts and habits of how things are done. Healthcare is constantly changing and new conditions such as AGS require providers and current practice to change. This project was designed after caring for an AGS patient where it was not known what medications were safe to administer and following discussions with key stakeholders at the clinical site. It was recognized that caring for patients with AGS requires specific knowledge to prevent exposure to triggering agents. An evidence-based educational intervention and site-specific cognitive aid were provided to improve provider knowledge and awareness of AGS and improve patient safety. The final step of Lewin's theory is refreezing which involves reinforcing and stabilizing change. It was anticipated that the provision of a site-specific medication safety list would enable providers to readily identify and avoid potential AGS-triggering agents in susceptible patients and improve patient safety.

Methods

This quality improvement project consisted of a preintervention survey (see Appendix A), educational intervention, introduction of a cognitive aid (see Appendix B), and post-intervention evaluation (see Appendix C). The cognitive aid created was a site-specific potential AGS triggering agent medication list which included commonly used medications in anesthesia.

Anesthesia providers attending a regularly scheduled department staff meeting were invited to complete a pre-intervention survey designed to assess their basic knowledge about Alpha-gal syndrome. All anesthesia providers at the facility site were asked to participate, including Certified Registered Nurse Anesthetists, Anesthesia Assistants, student registered nurse anesthetics, and anesthesiologists.

Design

This was a quality improvement project which implemented a site-specific medication list educational intervention to improve the confidence and knowledge of anesthesia providers caring for patients with AGS.

Translational Framework

The translational framework used for this project was the Johns Hopkins model for investigation. This model consists of first identifying a clinical problem. The second step of the Johns Hopkins model entails a thorough literature review to evaluate the current evidence about the problem and formation of a literature synthesis. Lastly, one must identify recommendations for change based on the evidence.

The clinical problem identified was a lack of awareness among anesthesia providers of Alpha Gal syndrome (AGS) and its clinical implications. In discussing this gap in knowledge and awareness, the PI found significant buy-in from key stakeholders for addressing the clinical issue. The second step of the Johns Hopkins model entailed a thorough literature review to evaluate the current evidence about AGS, the anesthetic implications of AGS, and evidence-based recommendations for improving clinical practice. The current evidence was reviewed, specifically focusing on AGS patient safety during the perioperative period.

This review of the existing evidence and collaboration with stakeholders identified that an educational in-service and creation of a cognitive tool would improve the safety of AGS patients during the perioperative period. Both interventions were implemented and evaluated for interval change.

Population

The population of interest was all anesthesia providers, as they all may encounter patients with AGS. All practicing anesthesia providers at the site of interest (Certified Registered Nurse Anesthetists, Anesthesiologist Assistants, Medical Doctors of Anesthesiology) were invited to participate in the project. Exclusion criteria included non-anesthesia personnel or anesthesia providers not practicing at the site. Any anesthesia providers at the site who chose not to participate were excluded. All anesthesia providers attending a previously scheduled departmental meeting were invited to attend. The PI also recruited additional participants by posting a flyer in the anesthesia lounge and via e-mail.

Setting

This project took place in the anesthesia department of a large tertiary care community hospital. This hospital is in an urban area, is private, not-for-profit, and has over 550 beds.

Project Implementation

A review of the literature revealed that patients with AGS are at high risk of exposure to triggering agents in the perioperative setting. A potential barrier to the safety of AGS patients was a lack of provider knowledge of AGS and potential AGS-triggering agents. Identification of these triggering agents for AGS patients is challenging because ingredients in medications can vary by manufacturer. Dunkman et al. (2019) and Nourian et al. (2023) recommend the creation of a medication safety list, maintained with pharmacy collaboration as new medications come on formulary.

The PI collaborated with key stakeholders at the facility site including the chief nurse anesthetist and an anesthesiologist to develop a site-specific medication safety list as a cognitive aid and an educational in-service. Commonly used medications were scanned for triggering ingredients and their safety in patients with AGS was marked “yes”, “no”, or “maybe” on the cognitive aid. This cognitive aid and an educational in-service were provided to participants at a staff meeting. Pre-intervention and post-intervention surveys were administered to anesthesia providers to assess for interval change in perceived understanding of AGS and recognition of potential AGS-triggering agents.

Instruments

The pre-intervention and post-intervention surveys were developed by the PI for the purpose of this project because no existing tool was identified in the extensive review of the literature. The questions were designed to assess provider AGS knowledge and confidence and included eleven statements on a 5-point Likert scale as well as demographic and experience questions. The survey created reflected key points from the review of the literature including: alternative names for AGS, etiology of AGS, triggering ingredients, common signs and

symptoms of AGS, the onset of reaction to triggering agent, and understanding that medication safety can depending on manufacturer. Demographics and experience questions included: highest anesthesia degree earned, years of anesthesia experience, whether the provider had previously cared for a patient with AGS, and whether the provider had received prior training for AGS in school or in the workplace.

Surveys were administered and results stored on Qualtrics, an online, password-protected survey tool. Participant responses were anonymous; however pre-intervention and post-intervention surveys were linked using a unique ID consisting of the last four digits of their phone number and first initial of mother's first name. Pre-intervention surveys (see Appendix A) were distributed via email by the chief CRNA and on a flyer in the anesthesia lounge with a QR code. Two weeks after the educational intervention, post-intervention surveys (see Appendix C) were distributed via the same method to assess for the presence of interval changes in participant knowledge.

The cognitive aid was developed in collaboration with key stakeholders in the anesthesia department. The PI attempted to contact the pharmacy department to collaborate on the creation and maintenance of the cognitive aid but was unsuccessful.

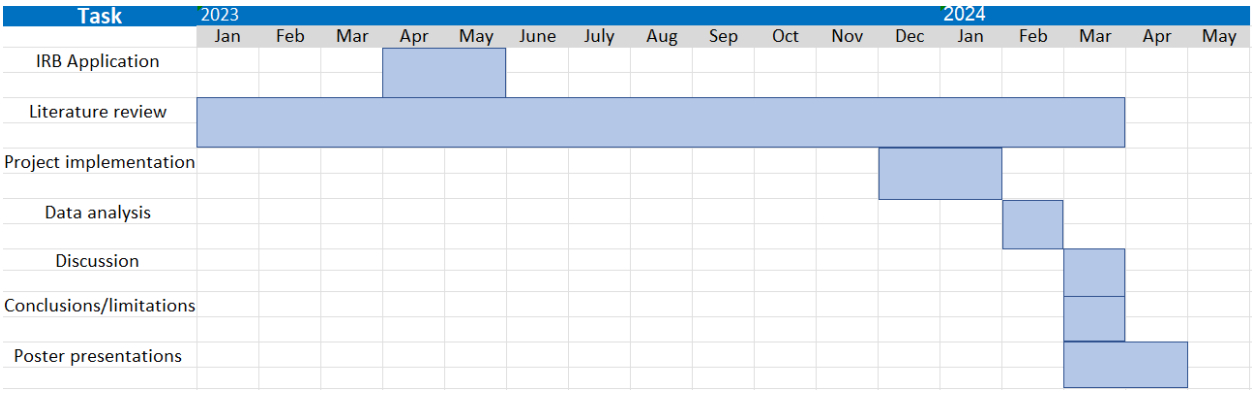
The most frequently used routine perioperative medications were identified by the PI and chief nurse anesthetist. These medications were each screened for AGS-triggering ingredients on the National Institutes of Health (NIH) sponsored drug database, DailyMed (dailymed.nlm.nih.gov). Each vial's National Drug Code (NDC) was identified and screened for the following ingredients: glycerin, gelatin, magnesium stearate, lactic acid, stearic acid, and any other recognized animal products. This process was previously described by Nourian, et al. (2023).

Medications that were not found to contain the known potential triggering agents: gelatin, glycerin, magnesium stearate, lactic acid, stearic acid, or any other animal product were deemed safe to use. Medications containing gelatin, glycerin, magnesium stearate, lactic acid, stearic acid, or any other animal product were deemed not safe to use. The cognitive aid was created in Excel and included the medication name, safety recommendation, triggering agent if applicable, manufacturer, and NDC code. Any relative notes were included, such as for heparin "large doses are higher risk. Make plan with pharmacy".

The educational in-service was a 15-minute PowerPoint presentation that took place at a previously scheduled anesthesia staff meeting. The presentation was created to address key topics from the review of the literature regarding AGS, and care of AGS patients specifically in the perioperative period. The in-service discussed the discovery of AGS, what animals contain alpha-gal, alternative names used for AGS, and AGS distribution, prevalence, how it relates to anesthesia, common signs and symptoms, onset of symptoms for reaction, treatment of reaction, potentially triggering agents, screening medications, and the site-specific medication list cognitive tool that was developed.

Timeline

Figure 1



IRB Approval

Permission was obtained from the site for implementation and a letter of support was written from the appropriate personnel at the site. This project was deemed a quality improvement project by the site and school; therefore IRB approval was not required. No incentives were given to participants to participate. No identifying information or protected health information was obtained.

Steps Implemented

Pre-intervention surveys were sent out by the nurse anesthetist chief via email and flyers in the breakroom. The PI then coordinated with the anesthesia team to decide on a date for intervention at an upcoming staff meeting. The educational in-service was conducted at the staff meeting and the cognitive aid was introduced to present anesthesia staff. The PowerPoint presentation and cognitive aid were emailed to the chief nurse anesthetist for distribution to the anesthesia team. Two weeks after the intervention post-intervention surveys were distributed in the same manner as pre-intervention surveys. The data was then analyzed with a statistician using Microsoft Excel with simple descriptive statistics.

The cognitive aid was compiled and color-coded via Excel then converted into a PDF to print on 8x10 paper. Each participant who attended the education in-service was provided with a cognitive aid which was also sent to the chief nurse anesthetist for distribution to the anesthesia team.

Pre-intervention and post-intervention surveys were created using the most pertinent information derived from the literature review to assess knowledge and confidence of anesthesia providers. To assess knowledge of commonly triggering agents, participants were asked to

identify out of fentanyl, red blood cell transfusion, Celebrex, and propofol, “Which of the following is most likely to cause a reaction to AGS”. Likert scale questions were utilized to assess knowledge of AGS and included “I know the common signs and symptoms of an AGS reaction”, “I know when the onset of an AGS reaction typically occurs”, “I know the alternative names for AGS”.

How data were collected

Data were collected from a total of 18 anesthesia providers who chose to participate. The data were collected utilizing Qualtrics, a password-protected online survey tool. No participant or patient identifiers were collected. Unique IDs consisting of the last four digits of a participant's phone number and first initial of their mother’s first name were collected.

Results

Eighteen anesthesia providers completed the pre-intervention survey. Baseline experience and demographics results are summarized in the table below (Table 1). The majority of participating providers were Certified Registered Nurse Anesthetists (83%). Most participating providers possessed a Master’s degree in Nurse Anesthesia (61%) and reported seven to ten years of experience in anesthesia (39%). Fifty-six percent of surveyed providers reported that they had previously cared for a patient with AGS. However, 89% reported that they had received no prior AGS training or education in school and 100% reported that they had received no AGS training in their workplace.

Table 1

Pre- Intervention Baseline Experience and Demographic Characteristics

Sample Characteristics	*n*	*%*
Anesthesia Degree		
Master's CRNA	11	61%
Doctorate CRNA	4	22%
Master's AA	2	11%
MDA	0	0%
Years of Anesthesia Practice		
0-3 years	5	28%
4-6 years	2	11%
7-10 years	7	39%
10+ years	4	22%
Cared for patient with AGS		
Yes	8	44%
No	10	56%
Received AGS training in school		
Yes	2	11%
No	16	89%
Received AGS training at work		
Yes	0	0%
No	18	100%

Prior to the educational intervention and introduction of the medication list, 50% of surveyed providers responded that they "somewhat agreed" or "strongly agreed" that they knew what Alpha Gal syndrome was. In the pre-survey, 83% of providers "somewhat disagreed" or "strongly disagreed" that they knew the alternative names for AGS. Most providers (61%) "strongly disagreed" or "somewhat disagreed" that they knew the common signs and symptoms of AGS in pre-surveys. When asked to identify which medication was most likely to cause a reaction for a patient with AGS, 39% correctly identified oral Celebrex pre-intervention.

Twenty-two percent of participants correctly identified the statement “Unfractionated heparin at low doses commonly causes reactions for patients with AGS” as false. Lastly, 72% of participants in the pre-intervention survey strongly agreed to understanding that “medication lists determining safety for Alpha Gal patients is subject to change as manufacturers may change ingredients at any time”.

Eighty medications were screened for triggering agents and included in the cognitive aid. Of the medications screened, 26 were found to be potentially triggering agents. These included common preoperative medications such as acetaminophen tablets, celecoxib capsules, gabapentin capsules, and aprepitant which contained stearic acid, magnesium stearate, glycerin, and gelatin. The Hydromorphone injection used at the time at this site contained lactic acid, a potential triggering agent. Heparin injection was included as a “NO” for safety with AGS patients with a note discussing large doses are higher risk and a recommendation to plan with pharmacy for anticoagulation if large doses are needed. Postoperative medications such as ondansetron tablets and oxycodone-acetaminophen tablets were also listed as “NO” for safety due to magnesium stearate and stearic acid.

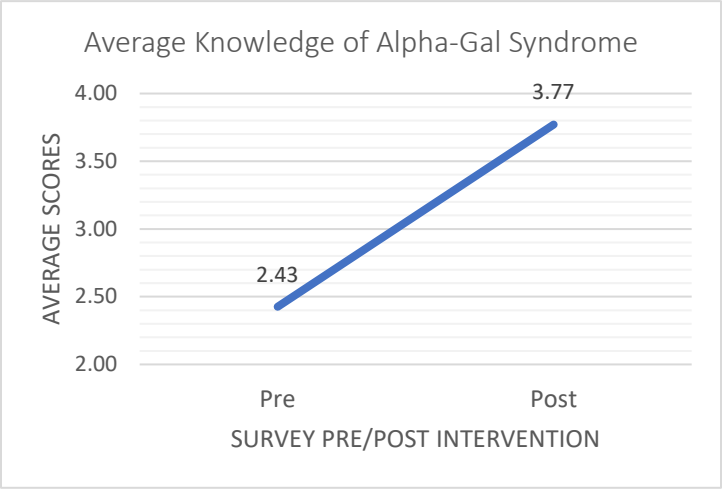
Following the intervention, 100% of survey respondents “strongly agreed” or “somewhat agreed” they knew what AGS was. One hundred percent of providers “strongly agreed” or “somewhat agreed” to knowing the alternative names for AGS. Again, 100% of providers “strongly agreed” or “somewhat agreed” to knowing the common signs and symptoms of AGS in post-intervention surveys. Post-intervention, 83% of providers correctly identified oral Celebrex as the most likely to cause a reaction in a patient with AGS. In the post-intervention survey, 100% of participants either “strongly agreed” or “somewhat agreed” to knowing that “medication lists determining safety for Alpha Gal patients is subject to change as manufacturers

may change ingredients at any time". Eighty-three percent of participants correctly identified the false statement, "Unfractionated heparin at low doses commonly causes reactions for patients with AGS" post-intervention.

A secondary outcome of confidence was assessed with one Likert scale question, "I feel confident I could safely treat a patient with Alpha-Gal Syndrome". Pre-survey surveys reported 67% of participants "strongly disagreed" or "somewhat disagreed" with this statement. Post-survey, 100% of participants "strongly agreed" or "somewhat agreed" feeling confident they could safely treat a patient with AGS.

Scores assessing knowledge from pre-intervention and post-intervention surveys were analyzed using Microsoft Excel. Likert scale questions were assigned a score of 1-5 for data analysis. Using the numericized data, scores for questions reflecting knowledge of AGS were averaged. An F-Test Two-Sample for variances was used to determine the two-tail was less than 0.05. Therefore, the variances were deemed not equal. A t-Test: two-sample assuming unequal variances was then performed and a p value of less than 0.05 indicated a significant difference in the means of knowledge scores from the pre-intervention and post-intervention surveys. Average knowledge score interval change is summarized in the chart below (Figure 2).

Figure 2



Barriers to Success

The low number of full-time anesthesia providers at this site was a barrier to success. This variable was not specifically address in surveys but should be considered. Initially an anesthesiologist with interest in AGS was assigned as a point person for the project. However, during project implementation, many staff including this anesthesiologist left the clinical site. The chief nurse anesthetist then facilitated project development and implementation.

Discussion

This project sought to increase safety of patients with Alpha Gal syndrome during the perioperative period through implementation of a site-specific medication list and evidence-based educational intervention. Pre-intervention survey findings demonstrate that 44% of anesthesia providers at this clinical site reported previously caring for a patient with AGS. This is consistent with previous studies reporting that up to 20% of the population in North Carolina may have serum IgE antibodies to alpha-gal (Chung et al., 2008; Commins et al., 2011; O'Neil et

al., 2007). It is likely that anesthesia providers practicing in Southeastern US states will care for patients with Alpha-Gal syndrome.

However, amongst surveyed providers prior to intervention, 61% “strongly disagreed” or “somewhat disagreed” they knew the common signs and symptoms of an Alpha Gal syndrome reaction. This is concerning, as 60-77.8% of patients with AGS report anaphylaxis (Wilson et al., 2020; Young et al., 2020). Without knowing that patients with AGS are at high risk of anaphylaxis, anesthesia providers may lack the increased vigilance that caring for a patient with AGS requires. Anaphylaxis is uncommon and the anesthetist may evaluate a wide differential diagnosis before arriving at this diagnosis. Anesthesia providers need to be aware of the high potential for a patient with AGS to develop anaphylaxis, rapidly recognize it, and initiate the appropriate treatment of epinephrine and other supportive measures in a timely/expeditious manner as the prompt administration of epinephrine is associated with better outcomes (Harper et al. 2018).

Prior to the introduction of the site-specific medication list and educational intervention 61% of anesthesia providers reported that they were unaware of the typical onset time of an allergic reaction to potential AGS-triggering agents in the perioperative period. AGS is unusual in that a reaction to orally administered alpha-gal may appear anywhere from ten minutes to six hours following exposure. Oral ERAS medications, such as Celebrex, are typically administered orally preoperatively. Celebrex was identified as an unsafe medication at this facility site, however 61% of surveyed anesthesia providers failed to identify orally-administered Celebrex as a potential AGS-triggering agents.

The goal of treatment in a patient with AGS is to prevent reaction. Pre-intervention, 50% of anesthesia providers surveyed did not report that they knew what ingredients may trigger a

reaction to AGS. Considering the likelihood that anesthesia providers in North Carolina will encounter AGS patients in their practice and that 56% reported actually previously caring for patients with AGS, this lack of knowledge places patients with AGS at high risk. Furthermore, less than 11% of surveyed providers had received training regarding AGS at school or in their workplace. Anesthesia providers deliver many medications concurrently and intravenously, creating the potential for rapid and severe reactions (Harper et al., 2018) and should be educated on the risks of these medications to a patient with AGS. Statistical analysis shows that this educational in-service and implementation of cognitive aid increased knowledge scores significantly.

Conclusion

AGS is relevant to anesthesia because many of the medications or medical products used during the perioperative period contain mammalian byproducts that have the carbohydrate alpha gal. Since reactions can occur hours after oral administration, ERAS medications given in the preoperative phase can cause a delayed reaction the intraoperative and postoperative phases. Thus, it is imperative that all preoperative, intraoperative, and postoperative providers must all be aware of this potential risk. Although all providers have a responsibility to patient care and safety during the perioperative stages, anesthesia is involved in preoperative, intraoperative, and postoperative care of a surgical patient. Therefore, they were the primary group of interest for the project. Anesthesia providers practicing in these areas especially need to be aware of the syndrome and how to avoid potential triggers and treat reactions for patients who suffer from it. In addition to vigilant administration of medications intraoperatively, anesthesia providers must be aware of the ongoing risks of pre- and postoperative medications.

This project identified a large knowledge gap in anesthesia providers regarding AGS. Many providers did not know what AGS was, let alone the etiology, common signs and symptoms, or what agents could trigger a reaction. The intervention of an educational in-service and creation of a medication safety list showed a statistically significant improvement in knowledge. As new information continues to be revealed and prevalence of AGS rises, anesthesia providers should stay current with what is being learned about AGS.

To continue to improve clinical practice, anesthesia providers should foster discussions with multidisciplinary teams to identify and avoid triggering agents for patients with AGS. Medical products such as hemostatic agents used intraoperatively can be triggering agents for patients with AGS. Education and cognitive aids designed for surgeons, operating room, preoperative, and postoperative staff would be beneficial, so all parties are aware of their role in avoidance of administering triggering agents. Many anesthesia providers are leaving full time positions to work part time or as contractors. Providers who are not full time at a site have less incentive to attend meetings or be engaged with evidence-based practice development at a site.

Prior to this project, there were no resources available for AGS at this facility. Implementation of the site-specific medication list is a start. However, formulations of one drug may vary manufacturer to manufacturer and the medication list will need to be updated. Anesthesia providers often will not have the time to look up each medication's ingredient list and scan for triggering agents. Therefore, pharmacy involvement in this process would be ideal as they could update the medication list when new medications come on formulary and help to decrease surgical delays.

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Appendix A

Alpha-Gal Syndrome Pre-Intervention Survey

*Please write the last four digits of your phone number: _____

*First initial of your Mother's first name _____

Circle your answer:

1. What is your anesthesia degree?	Certificate	Master's Nurse Anesthesia	Doctorate Nurse Anesthesia	Doctor of Medicine Anesthesiology	N/A
2. How many years of anesthesia practice do you have? (not including school)	0-3 years	4-6 years	7-10 years	10+ years	
3. Have you cared for a patient with Alpha Gal Syndrome (AGS)?	Yes	No			
4. In school, did you receive any training regarding Alpha Gal Syndrome?	Yes	No			
5. Since beginning your clinical practice have you received any formal education/training regarding Alpha Gal Syndrome?	Yes	No	N/A		
6. Which of the following is most likely to cause a reaction for a patient with AGS?	IV Fentanyl	Red Blood Cell Transfusion	PO Celebrex	IV Diprivan (Propofol)	
7. True or false: Unfractionated heparin at low doses commonly causes reactions for patients with Alpha Gal Syndrome	True	False			

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree

1. I know what Alpha-Gal syndrome is	1	2	3	4	5
2. I know the alternative names for AGS	1	2	3	4	5
3. I know the etiology of AGS	1	2	3	4	5
4. I know what ingredientss or products can trigger a reaction in a person with AGS	1	2	3	4	5
5. I know the common signs and symptoms of an AGS reaction	1	2	3	4	5
6. I know when a reaction to AGS will most commonly occur in the perioperative period	1	2	3	4	5
7. I feel confident I could safely treat a patient with AGS	1	2	3	4	5
8. I know what resources my facility has for treating patients with AGS	1	2	3	4	5
9. I understand that medication lists determining safety for AGS patients is subject to change as manufacturers may change ingredients at any time	1	2	3	4	5

Appendix B

Alpha-gal Syndrome Medication Safety per Manufacturer. AGS is a tick-borne syndrome to mammalian meat products containing alpha-gal carbohydrates. The following ingredients should be avoided: glycerin, gelatin, lactic acid, stearic acid, magnesium stearate if animal derived. Each medication should be scanned (using the NDC for each vial on https://dailymed.nlm.nih.gov) for containing these ingredients and the manufacturer may be contacted to determine if animal or plant derived. This list is intended for Healthcare professionals.

Created November 2023 *Disclaimer: Information is subject to change at any time.

Drug/Product Name	safety	Ingredient	Manufacturer	NDC code	Notes
Acetaminophen 500mg tablet	NO	Stearic acid	Reliable 1 Laboratories LLC	69618-011-01, 69618-011-10	
Acetaminophen 500mg tablet	NO	Magnesium stearate, glycerin, gelatin	Strive Pharmaceuticals Inc	70692-117-06, 70692-117-41	
Acetaminophen 500mg tablet	YES		Alvio Medical Products, LLC		
Albumin	YES		CSL Behring AG	44206-310-25, 44206-310-50, 44206-310-90, 44206-310-91	
Aprepitant capsule	NO	Gelatin	Torrent Pharmaceuticals Limited	13668-591-80, 13668-591-81, 13668-591-82, 13668-592-83	
Atropine Sulfate Injection	YES		American Regent, Inc.	0517-1001-01, 0517-1001-25, 0517-1004-01, 0517-1004-25	
Cefazolin	YES		Apotex Corp	60505-6142-0, 60505-6142-5, 60505-6231-0, 60505-6231-5	
Celecoxib capsule	NO	Magnesium stearate, Gelatin	SYDON LABS LLC		
Celecoxib capsule	NO	Magnesium stearate, Gelatin	Alembic Pharmaceuticals Inc.		
Celecoxib capsule	NO	Magnesium stearate, Gelatin	Amneal Pharmaceuticals LLC		
Celecoxib capsule	NO	Gelatin	Aurobindo Pharma Limited		
Celecoxib capsule	NO	Magnesium stearate, Gelatin	Cadila Pharmaceuticals Limited		
Dexamethasone Injection	YES		Hikma Pharmaceuticals USA Inc.	0641-0367-21, 0641-0367-25, 0641-6145-01, 0641-6145-25	
Diphenhydramine Injection	YES		Fresenius Kabi USA, LLC	63323-664-00, 63323-664-01	
Ephedrine Injection	YES		Nexus Pharamaceuticals Inc.	14789-250-07, 14789-250-10	
Epinephrine Injection	YES		Hospira, Inc.	0409-4933-01, 0409-4933-11	
Etomidate Injection	YES		Eugia US LLC	55150-221-10, 55150-222-20	
Etomidate Injection	YES		Fosun Pharma USA Inc	72266-146-01, 72266-146-10, 72266-147-01, 72266-147-10	
Etomidate injection	YES		Fresenius Kabi USA, LLC	65219-445-01, 65219-445-10, 65219-447-02, 65219-447-20	
Fentanyl Injection	YES		Civica, Inc.	72572-170-01, 72572-170-25, 72572-171-01, 72572-171-25	
Fentanyl Injection	YES		Hikma Pharmaceuticals USA Inc.	0641-6024-01, 0641-6024-10, 0641-6025-01, 0641-6025-10	
Fentanyl Injection	YES		Phlow Corp.	81565-205-01, 81565-205-02	
Fentanyl Injection	YES		Akorn	17478-030-02, 17478-030-05, 17478-030-10, 17478-030-20,	
Fentanyl Injection	YES		Cantrell Drug Company	52533-025-05	
Gabapentin capsule	NO	Gelatin	ACI Healthcare USA, Inc.		
Gabapentin capsule	NO	Gelatin	Actavis Pharma, Inc.		
Gabapentin capsule	NO	Gelatin	Amneal Pharmaceuticals LLC		Gelatin not listed in ingredients but characteristics state HARD GELATIN capsule
Gabapentin capsule	NO	Gelatin	Amneal Pharmaceuticals of New York LLC		Gelatin not listed in ingredients but characteristics state HARD GELATIN capsule
Glycopyrrolate Injection	YES		Meitheal Pharmaceuticals Inc.	71288-414-01, 71288-414-02, 71288-414-03, 71288-414-04	
Heparin injection, solution	NO	porcine intestinal mucosa	McKesson Corporation dba SKY Packaging	63739-900-12, 63739-900-26, 63739-901-14, 63739-901-28	Large doses are higher risk. Make plan with pharmacy
Heparin injection, solution	NO	porcine intestinal mucosa	Fresenius Kabi USA, LLC	63323-517-01, 63323-517-74, 63323-518-01, 63323-518-77.	Large doses are higher risk. Make plan with pharmacy
Hydralazine Injection	YES		Fresenius Kabi USA, LLC	63323-614-00, 63323-614-01	
Hydromorphone HCl injection	YES		Cantrell Drug Company	52533-005-45	some sources say hydromorphone Hcl injection may contain lactic acid, though none of these listed it
Hydromorphone HCl injection	YES		Akorn	17478-540-01, 17478-540-05, 17478-540-50	
Hydromorphone HCl injection	YES		Hikma Pharmaceuticals USA Inc.	0641-6151-01, 0641-6151-25	
Hydromorphone HCl injection	YES		Fresenius Kabi USA, LLC	76045-009-00, 76045-009-03, 76045-009-05, 76045-009-10	
Hydromorphone HCl injection	NO	Lactic Acid	Hospira, Inc.	0409-1283-03, 0409-1283-04, 0409-1283-05, 0409-1283-09	
Hydromorphone HCl tablet	NO	Magnesium stearate	ETHEX Corporation	58177-449-04, 58177-449-09, 58177-449-11, 58177-820-04...	
Hydromorphone HCl tablet	NO	Magnesium stearate	Aurolife Pharma, LLC	13107-107-01, 13107-107-05, 13107-107-20, 13107-107-99...	
Hydromorphone HCl tablet, extended release	NO	Magnesium stearate	Ascent Pharmaceuticals, Inc.	43602-266-05, 43602-266-30, 43602-267-05, 43602-267-30	
Hydromorphone HCl solution	NO	Glycerin	American Health Packaging	42858-304	
Ketamine injection	YES		AuroMedics Pharma LLC	55150-438-10, 55150-439-10, 55150-440-10	
Ketamine injection	YES		Civica, Inc.	72572-320-01, 72572-320-10, 72572-321-01, 72572-321-10	
Ketamine injection	YES		Hikma Pharmaceuticals USA Inc.	0143-9508-01, 0143-9508-10, 0143-9509-01, 0143-9509-10	

Ketamine injection	YES		Par Pharmaceutical, Inc.	42023-113-10, 42023-114-10, 42023-115-10	
Ketoralac Injection	YES		Fresenius Kabi USA, LLC	63323-161-00, 63323-161-01, 63323-162-00, 63323-162-01	
Labetalol Hydrochloride Injection	YES		Almaject, Inc.	72611-734-01, 72611-738-01	
Lidocaine HCl Injection	YES		Hospira, Inc.	0409-4275-01, 0409-4275-16, 0409-4276-01, 0409-4276-02	
Metoprolol Tartrate Injection	YES		Baxter Healthcare Corporation	36000-033-10	
Midazolam Injection	YES		Cantrell Drug Company	52533-001-31	
Midazolam Injection	YES		Cantrell Drug Company	52533-001-75	
Midazolam Injection	YES		Cantrell Drug Company	52533-157-75	
Midazolam Injection	YES		Cantrell Drug Company	52533-157-45	
Midazolam Injection	YES		Cantrell Drug Company	52533-001-77	
Midazolam Injection	YES		Hikma Pharmaceuticals USA Inc.	0641-6056-01, 0641-6056-10, 0641-6057-01, 0641-6057-10	
Morphine Sulfate Injection	YES		Hikma Pharmaceuticals USA Inc.	0641-6125-01, 0641-6125-25, 0641-6126-01, 0641-6126-25	
Neostigmine Injection	YES		Dr.Reddy's Laboratories Inc	43598-528-11, 43598-528-36, 43598-529-11, 43598-529-36	
Ondansetron HCl injection	YES		Apotex Corp.	60505-6130-0, 60505-6130-5	
Ondansetron HCl injection	YES		Mylan Institutional LLC	67457-769-00, 67457-769-02	
Ondansetron HCl injection	YES		Steriscience Specialties Private Limited	82449-201-01	
Ondansetron HCl injection	YES		WOCKHARDT LIMITED	55648-726-01, 55648-727-01	
Ondansetron HCl tablet, film coated	NO	Magnesium stearate	Aurobindo Pharma Limited	65862-187-02, 65862-187-05, 65862-187-10, 65862-187-30,	
Ondansetron HCl tablet, film coated	NO	Magnesium stearate	Dr. Reddy's Laboratories Limited	55111-153-01, 55111-153-05, 55111-153-13, 55111-153-30...	
Ondansetron tablet, orally disintegrating	NO	Magnesium stearate	Sun Pharmaceutical Industries, Inc.	62756-130-01, 62756-130-02, 62756-131-01, 62756-131-02...	
Oxycodone HCl tablet, film coated, extended release	NO	Magnesium stearate	Amneal Pharmaceuticals NY LLC	69238-2294-1, 69238-2295-1, 69238-2296-1, 69238-2300-1	
Oxycodone HCl tablet, film coated, extended release	NO	Magnesium stearate	KVK-Tech, Inc.	10702-801-01, 10702-803-01, 10702-805-01	
Oxycodone-Acetaminophen tablet	NO	Stearic acid	Mayne Pharma Inc.	68308-475-47, 68308-480-47	
Oxycodone-Acetaminophen tablet	NO	Stearic acid	SpecGx LLC	0406-0512-01, 0406-0512-05, 0406-0512-23, 0406-0512-62	
Phenylephrine HCl Injection	YES		Cantrell Drug Company	52533-130-79	
Phenylephrine HCl Injection	MAYBE		SCA Pharmaceuticals	70004081012	NDC not found on Dailymed. Check with manufacturer
Propofol (Diprivan) Injection	YES	Glycerin (plant based)	Fresenius Kabi USA, LLC	63323-269-10, 63323-269-22, 63323-269-29, 63323-269-30	
Propofol Injection	MAYBE	Glycerin	Dr. Reddy's Laboratories, Inc.	43598-265-20, 43598-265-25, 43598-265-58, 43598-548-21	Check with manufacturer. Glycerin may be plant or animal based.
Propofol Injection	MAYBE	Glycerin	Actavis Pharma, Inc.	0591-2136-51, 0591-2136-55, 0591-2136-57, 0591-2136-68	Check with manufacturer. Glycerin may be plant or animal based.
Propofol Injection	MAYBE	Glycerin	Civica, Inc	72572-590-01, 72572-590-10, 72572-601-01, 72572-601-20...	Check with manufacturer. Glycerin may be plant or animal based.
Remifentanil Injection	YES		Mylan Institutional LLC	67457-198-00, 67457-198-03, 67457-198-05, 67457-198-10	
Succinylcholine Injection	YES		Indoco Remedies Limited	14445-407-10, 14445-407-25	
Succinylcholine Injection	YES		Camber Pharmaceuticals, Inc.	31722-981-10, 31722-981-31	
Sugammadex injection (Bridion)	YES		Merck Sharp & Dohme LLC	0006-5423-02, 0006-5423-05, 0006-5423-12, 0006-5423-15	
Vasopressin Injection (Vasostrict)	YES		Par Pharmaceutical, Inc.	42023-164-01, 42023-164-10, 42023-164-25, 42023-190-01	
Vecuronium Injection	YES		AuroMedics Pharma LLC	55150-235-01, 55150-235-10, 55150-236-01, 55150-236-20	
Vecuronium Injection	YES		Fresenius Kabi USA, LLC	63323-781-10, 63323-781-21, 63323-782-20, 63323-782-23	

Appendix C

Alpha-Gal Syndrome Post-Intervention Survey

*Please write the last four digits of your phone number: _____

*First initial of your Mother's first name _____

Circle your answer:

8. What is your anesthesia degree?	Certificate	Master's Nurse Anesthesia	Doctorate Nurse Anesthesia	Doctor of Medicine Anesthesiology	N/A
9. How many years of anesthesia practice do you have? (not including school)	0-3 years	4-6 years	7-10 years	10+ years	
10. Have you cared for a patient with Alpha Gal Syndrome (AGS)?	Yes	No			
11. In school, did you receive any training regarding Alpha Gal Syndrome?	Yes	No			
12. Since beginning your clinical practice have you received any formal education/training regarding Alpha Gal Syndrome?	Yes	No	N/A		
13. Which of the following is most likely to cause a reaction for a patient with AGS?	IV Fentanyl	Red Blood Cell Transfusion	PO Celebrex	IV Diprivan (Propofol)	
14. True or false: Unfractionated heparin at low doses commonly causes reactions for patients with Alpha Gal Syndrome	True	False			

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
10. I know what Alpha-Gal syndrome is	1	2	3	4	5
11. I know the alternative names for AGS	1	2	3	4	5
12. I know the etiology of AGS	1	2	3	4	5
13. I know what ingredientss or products can trigger a reaction in a person with AGS	1	2	3	4	5
14. I know the common signs and symptoms of an AGS reaction	1	2	3	4	5
15. I know when a reaction to AGS will most commonly occur in the perioperative period	1	2	3	4	5
16. I feel confident I could safely treat a patient with AGS	1	2	3	4	5
17. I know what resources my facility has for treating patients with AGS	1	2	3	4	5
18. I understand that medication lists determining safety for AGS patients is subject to change as manufacturers may change ingredients at any time	1	2	3	4	5