Alpha Gal Syndrome in the Perioperative Environment

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A Project Report Submitted to

the Faculty of The School of Nursing at

The University of North Carolina at Greensboro

in Partial Fulfillment

of the Requirements for the

Doctorate in Nursing Practice

Greensboro

2022

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Abstract

Background: Alpha gal syndrome (AGS) is an allergy acquired from the bite of the lone star tick. This allergy manifests as a sensitivity to red meat, medicines, and implants derived from mammalian sources. Many of the medications that induce AGS are commonly used in the perioperative environment. Alpha gal syndrome can trigger serious, life-threatening reactions and it is crucial for health care providers to possess knowledge about AGS, its triggers, treatment, and prevention. **Purpose:** The purpose of this DNP project was to evaluate if an educational presentation and reference guide about alpha gal syndrome increased health care providers knowledge about how to recognize and manage the syndrome in their patients. **Methods:** The project used a quasi-experimental design to evaluate the impact of an educational session and educational resources on healthcare providers' knowledge of alpha gal syndrome. The intervention involved a 15-minute multimedia presentation that provided comprehensive information about AGS. Additionally, an online resource was created that contained information on medications capable of triggering alpha gal responses in various operative settings. **Recommendations and Conclusion:** Results showed no significant change in test scores for health care providers after intervention and overall higher mean scores than those reported in the literature. Health care providers may be becoming more aware of alpha gal syndrome through self-education or peer communication. Adaptation of existing protocols is a next step in managing care for alpha gal patients.

Key Words: alpha gal, anaphylaxis, IgE, allergy, tick bite, perioperative care.

Background and Significance

Galactose-alpha-1,3-galactose, also known as alpha gal, is a carbohydrate specific to non-primate mammal tissue. The alpha gal carbohydrate triggers a type I, or anaphylactic reaction, in susceptible patients who ingest products from a mammalian source such as beef, pork, or any red meat. Alpha gal sensitivity develops in people who have suffered a bite from the lone star tick (*Amblyomma americanum*) (Commins & Platts-mills, 2010; Mackay et al., 2014).

The allergic reaction to alpha gal, known as alpha gal syndrome or AGS, was initially discovered in the population of patients receiving cetuximab, a chemotherapeutic agent frequently used for treatment of colorectal cancer (O'Neil et al., 2007). Published data for cetuximab indicated the risk of anaphylaxis to be three percent. However, patients in the southeastern United States were demonstrating anaphylaxis at a rate as high as 22% (O'Neil et al., 2007). Additionally, patients were suffering the high rate of anaphylaxis even on their first dose of cetuximab (Wen et al., 2021). Chung et al. (2008), postulated that the reactive patients had preexisting antibodies to alpha gal which caused their malady.

Patients with an allergy to alpha gal will exhibit symptoms of stomach pain, urticaria, itching, feelings of throat closing or itching, and anaphylaxis (Altshuler et al., 2021; “Diagnosing a Crisis”, 2021; Patel & Iweala, 2020). Unlike anaphylactic reactions from chemicals such as bee venom, reactions to alpha gal are delayed by as much as six hours (Patel & Iweala, 2020). Because carbohydrates are broken down quickly in the digestive process researchers theorize the mechanism by which an alpha gal reaction is triggered is complex (Mackay et al., 2014). Alpha gal carbohydrates can be incorporated into glycolipids which are then formed into chylomicrons (ultra-low-density lipoproteins). The new chylomicrons are then released systemically and trigger a type I allergic reaction (Mackay et al., 2014). According to Commins and Platts-Mills

(2010), cuts of meat with more adipose tissue, such as beef and pork, trigger a faster and more severe reaction further supporting this proposed mechanism of action.

The range of the lone star tick (*Amblyomma americanum*) has significant overlap with the area of the country in which patients were experiencing elevated rates of anaphylaxis attributed to cetuximab (Thomas et al., 2020). Mackay et al., (2014) proposed that the bite of the tick gives an immunogenic exposure to the alpha gal carbohydrate. Patients with AGS in the southeastern United States tended to have multiple exposures to tick bites and development of fever and rash after the bite were associated with higher incidences of AGS (Thomas et al., 2020).

Diagnosis of alpha gal syndrome can be done with skin prick testing or intradermal testing (Mackay et al., 2014, pp. 206-209; Strickler, 2017; Thomas et al., 2020). The intradermal testing methodology gives more pronounced results than skin prick testing, which typically generates a smaller than 4 mm skin wheal (Mackay et al., 2014, pp. 206-209). Additionally, assessment of symptoms is important in the diagnosis of AGS. As discussed above, patients with AGS experience a delayed onset (2-6 hours) of symptoms after eating beef, pork, lamb, or goat meat (Patel & Iweala, 2020). Symptoms range from upset stomach, to hives, to anaphylaxis. These symptoms are not elicited by eating chicken, turkey, or fish (Altshuler et al., 2021; "Diagnosing a Crisis," 2021; Patel & Iweala, 2020).

Beyond cetuximab, alpha gal is present in a large variety of pharmaceutical products (Dunkman et al., 2019). In some cases, identifying these products is straightforward, i.e., porcine derived heparin. However, in many cases potentially alpha gal containing ingredients are non-active and thus not listed in medication packaging (Dunkman et al., 2019).

Healthcare providers are largely unaware of AGS, its management, and detection (Farmer et al., 2021; Thomas et al., 2020); however, understanding AGS is critical to safe patient

management, particularly in the southeastern United States. Specifically, anesthesia providers should have an in depth understanding of AGS reactions as patients in their care may be unable to report symptoms. Furthermore, providers should be alert for reported allergies to mammalian meat products, as these symptoms may be reported without a diagnosis of AGS. This project aims to increase health care providers' knowledge about AGS, their ability to recognize triggering agents, and their ability to manage patients with AGS.

Purpose

The purpose of this DNP project was to evaluate if an educational presentation and reference guide about alpha gal syndrome increased health care providers knowledge about how to recognize and manage the syndrome in their patients.

Review of Current Evidence

Alpha Gal syndrome (AGS) is an acquired hypersensitivity allergy that develops after exposure to galactose-α-1,3-galactose (alpha gal) and is mediated by immunoglobulin E (IgE) antibodies (Dunkman et al., 2019; Thomas et al., 2020). This antibody is implicated in development of anaphylaxis from two sources: medications and dietary red meat. Reactions to cetuximab show an immediate onset while reactions to red meat exhibit a delayed onset (Dunkman et al., 2019; Thomas et al., 2020).

In 2007, O'Neil et al. evaluated anecdotal evidence that patients in North Carolina and Virginia suffered hypersensitivity reactions while receiving cetuximab at a rate far higher than the national average. They discovered that 22% of patients suffered anaphylactoid reactions compared to the national average of 3%. Many of the impacted patients reported spending a large

amount of time outdoors for work. The geographic distribution of patient's residences and workplaces correlates closely with the range of the lone star tick (*Amblyomma americanum*) (Altshuler et al., 2021; Thomas et al., 2020).

When the lone star tick bites, saliva is secreted into the host. The saliva contains alpha gal carbohydrates in high concentrations and is likely the triggering agent for the development of alpha gal syndrome (Altshuler et al., 2021; Bianchi et al., 2019; Patel et al., 2020; Thomas et al., 2020; Wolfe & Blunt, 2021. Altshuler et al. (2021) postulate that Th-2 mediated immunity or class switching of IgE are responsible and facilitated by prostaglandin E2. The Th-2 cells are a subset of T-helper cells involved in immune response. When someone is bitten by a tick Th-2 cells become activated and release cytokines interlukin-4, and interlukin-13 (Koyasu & Moro, 2011). These cytokines trigger class switching in B cells which leads to IgE antibody production instead of IgG or IgM antibodies (Mak et al., 2014).

Risk of developing AGS is impacted by a person's blood type (Patel & Iweala, 2020). The IgE antibody concentration in individuals with type B or AB blood were much lower than those with O and A type blood. Alpha gal syndrome reactions amongst people who have type B or AB blood were five times lower than expected although mechanisms for this are not yet explored (Brestoff et al., 2018).

Clinical presentation of AGS may be multifactorial and varied. Thomas et al. (2020) and Bianchi et al. (2019) give the following cluster of symptoms as typical for the disorder:

A) Sufferers will experience an onset in adulthood after having formerly tolerated eating red meat or mammalian products.
B) They will experience symptoms ranging from generalized gastroenteritis to those typical of anaphylaxis, i.e., runny nose, urticaria, angioedema and cardiovascular collapse

(Bianchi et al., 2019; Thomas et al., 2020). Onset of symptoms begin 2-6 hours after consuming mammalian meat products, although some patients report faster onset of some symptoms, especially after exercise ("Diagnosing a Crisis," 2021).

C) Laboratory testing will show a positive result for lgE for alpha gal with antibodies greater than 2 IU/ml.

D) Patients will demonstrate improvement in symptoms after diet modification and restriction (Thomas et al., 2020).

Cardiovascular Implications

As the literature base related to AGS expands, novel implications of the syndrome are being documented. Current literature is investigating an association between AGS and cardiovascular disease (Bianchi et al., 2019; Mozzicato et al., 2014; Thomas et al., 2020). Patients testing positive for IgE to alpha gal demonstrated more severe coronary artery disease than those with negative test results (Bianchi et al., 2019, Mozzicato et al., 2014; Thomas et al., 2020). The IgE specific for alpha gal may increase atherosclerosis and plaque formation intravascularly (Patel & Iweala, 2020). Vernon et al. (2022) assert that repeated alpha gal reactions promote increased concentrations of circulating inflammatory mediators, in turn damaging arterial interna, ultimately leading to atherosclerosis and vascular disease (Thomas et al., 2020). It is a possibility, though not established, that patients with AGS who tolerate eating red meat without deleterious effects are also at an increased risk of developing cardiovascular disease (Bianchi et al., 2019). More research is needed in the area, and it is too early to make clinical recommendations at this time.

Alpha gal syndrome also has implications for patients who have valvular cardiovascular disease (Patel & Iweala, 2020). Surgical treatment for valvular heart disease involves implantation of either a mechanical prosthetic or bioprosthetic valve to replace the diseased native valve. In two reported cases patients with AGS suffered early degradation of their bioprosthetic valves (Hawkins et al., 2016). One to two years after diagnosis with AGS the patients began to experience chest pain and valvular regurgitation because of failure of the implanted valve(s). Ultimately, the patient's valves were replaced with mechanical valves (Hawkins et al., 2016). More dangerously, two other patients suffered anaphylaxic reactions after implantation of bioprosthetic valves a (Mozzicato et al., 2014). Over time, the two patients who initially suffered anaphylaxis were able to tolerate their new bioprosthetic valves after supportive care in the acute post operative period (Mozzicato et al., 2014). Decellularized valves may be viable choices for patients with AGS as their levels of alpha gal are undetectable on laboratory analysis (Dunkman et al., 2019).

Pharmacologic Implications

Alpha gal syndrome carries implications for the pharmacologic treatment of patients. As previously discussed, patients with AGS are at an increased risk of anaphylaxis when receiving cetuximab, but this risk applies to many medications (Wolfe & Blunt, 2021). Heparin is often derived from bovine or porcine sources, and thus likely carries some amount of alpha gal antigen. Therefore, patients with previously diagnosed AGS may be more likely to have a hypersensitivity reaction when given high dose heparin, as is commonly done in cardiovascular surgery (Hawkins et al., 2021). Studies show that patients with AGS had a reaction to heparin at

a rate of 50% while the general population had a rection at a rate of 0.19% (Hawkins et al., 2021).

Evaluating other pharmacologic agents as triggers of AGS is more challenging than in the case of heparin. This is due to the role of inactive ingredients that are derived from mammalian sources. Dunkman et al. (2019) give the following inactive ingredients and their common derivative medications:

- Stearic acid: Oxycodone tablets
- Lactic acid: hydromorphone injection, haloperidol injection,
- Magnesium stearate: acetaminophen tablets, OxyContin,
- Glycerin: ibuprofen suspension, methadone solution, acetaminophen liquid
- Gelatin: Alvimopan, aprepitant celecoxib, pregabalin, gabapentin capsules, lidocaine patch, serriform powder

It is important to identify patients with AGS in the perioperative setting so that triggering agents are avoided, and the list of differential diagnoses is shorter in the case of an adverse reaction. This is challenging as the mean time from onset of symptoms to diagnosis is 7.5 years ("Diagnosing a Crisis," 2021), and patients may believe their dietary symptoms have no relevance to medication allergies.

Suspicion of AGS is warranted if the patient lists allergies such as red meat, beef, or pork in the medical record. A documented allergy to cetuximab should trigger follow-up questions on patient interview. Additionally, increased suspicion for AGS should be leveled when patients have lived in the Southeastern United States or report a history of tick bite (Dunkman et al., 2019).

Anaphylaxis

According to Rutkowski et at. (2012), there is lack of consensus in the literature about how anaphylaxis is defined. Broadly it is an acute hypersensitivity reaction that may result in death without treatment (Sampson et al., 2006). Typical clinical features include an acute onset, integumentary system changes, respiratory and or cardiac collapse, or some combination of these symptoms (Rutkowski et al., 2012; Sampson et al., 2006). Food may be a triggering agent of anaphylaxis, but insect venom and medications are also common triggers (Rutkowski et al., 2012). During anesthesia, neuromuscular blocking agents are the most common trigger (Mali, 2012).

Treatment for acute hypersensitivity reactions related to AGS are the same as those for anaphylaxis triggered by any other agent. First, remove the triggering agent if possible (Mali, 2012). Then support the patient's airway, breathing, and circulation and treat with epinephrine and histamine one and two blockers (Dunkman et al., 2019; Mali, 2012)). Next, perform cardiopulmonary resuscitation (CPR) if required and establish intravenous access to administer one to two liters of fluid for an adult (Rutkowski et al., 2012).

For chronic management of AGS, the primary intervention is counseling patients to avoid any triggering agents (Thomas et al., 2020). The secondary intervention is the prescription of an epinephrine injector in the outpatient setting. Avoiding mammalian meat products is effective in preventing symptoms in 80% of patients. In the 20% of patients whose symptoms did not resolve by avoiding red meat alone, most had symptom relief by avoiding dairy and eggs (Thomas et al., 2020).

Health care providers' knowledge about AGS can be enhanced through education (Farmer et al., 2021). A protocol for how to identify, manage, and treat patients who have AGS

is needed to reduce perioperative risk related to the syndrome. This is especially important in health care facilities in the southeastern United States, as higher rates of AGS are seen in the native environment of the lone star tick.

Conceptual Framework

The Knowledge to Action (KTA) framework served as the conceptual framework for this project because it addresses how information is disseminated from the literature into practice. There is significant delay in, and mistranslation of, information as it makes its way from the research area and into the clinical area (Graham et al., 2006). Patients are not being offered the best care because of these delays and inadequacies. One barrier of establishing a knowledge transfer framework is the use of non-standard language across applied research (Graham et al., 2006). Standardizing to the simpler Knowledge to Action verbiage forms a less specific, more variable language that can help reduce clutter and confusion (Graham et al., 2006).

The KTA process encompasses two concepts, creation of knowledge and action (Graham et al., 2006). The knowledge phase is typically illustrated as a triangle or funnel (see appendix A). Knowledge begins with a question, or knowledge inquiry. Next, through research of the literature and other methods knowledge is synthesized, collected, and concentrated into its relevant components (Graham et al., 2006). The final component of the knowledge to action process is using tools, practice guidelines, and products. Some of the nuances of the prior step are removed in favor of simple, clear recommendations to impact stakeholder actions. Five questions should be answered in this step: (a) what should be disseminated; (b) to whom should it be disseminated; (c) by whom should it be disseminated; (d) how should it be disseminated; (e) with what effect should it be disseminated (Graham et al., 2006)?

The action cycle has seven dynamic stages: identifying the problem, adapting knowledge, assessing barriers, implementing, monitoring, evaluating, and sustaining (Graham et al., 2006). For the purpose of this project, the problem was identified through observation of clinical anesthesia practice and through literature review. Adapting knowledge was to be accomplished through offering information about how to identify alpha gal syndrome in perioperative patients and how to manage their care. Barriers were multifactorial and included knowledge deficit, the occult nature of alpha gal syndrome, and the limited time a provider has to complete the preoperative interview and assessment. This project aims to break down the barrier of knowledge deficit. The baseline assumption is that people will make better decisions if they have access to better information. Outcomes were evaluated by collecting empirical data about health care providers' knowledge about AGS prior to the educational intervention and after using a pre-post study format.

Translational Framework

Plan

The Plan-Do-Study-Act (PDSA) framework is a well-established quality improvement model widely used in healthcare setting (Moen & Norman, 2010; "Plan-Do-Study-Act, 2020). It provides a systematic approach to implementing and evaluating changes in practice to achieve desired outcomes (Moen & Norman, 2010). In the context of this paper, the PDSA framework serves as the translational foundation for designing and evaluating the educational intervention aimed at improving knowledge of alpha gal syndrome among healthcare providers. The planning phase of the project involved conducting a comprehensive literature review on alpha gal syndrome, its triggers, treatment, and preventative measures. The literature review aimed to

gather evidence-based information to inform the development of the educational intervention and the creation of the information reference.

Summary of Literature

Alpha Gal syndrome (AGS) is an acquired hypersensitivity reaction triggered through activation of immunoglobulin E (IgE) antibodies to carbohydrate galactose-α-1,3-galactose, alpha gal (Dunkman et al., 2019; Thomas et al., 2020). This syndrome is characterized by anaphylactic reactions to medications and dietary consumption of red meat. The prevalence of AGS is correlated with the presence of the lone star tick in certain regions (Altshuler et al., 2021; Thomas et al., 2020).

Patients with AGS may experience symptoms across a spectrum from generalized gastroenteritis to anaphylaxis including urticaria, angioedema, and cardiovascular collapse (Bianchi et al., 2019; Thomas et al., 2020). Laboratory testing reveals elevated levels of IgE antibodies specific to alpha gal, confirming the diagnosis (Thomas et al., 2020).

AGS is associated with cardiovascular implications, with patients testing positive for alpha gal specific IgE antibodies suffering coronary artery disease at a higher rate than those with negative test results (Bianchi et al., 2019; Mozzicato et al., 2014; Thomas et al., 2020). Furthermore, patients with AGS who undergo surgical treatment for valvular heart disease using bioprosthetic valves may suffer anaphylaxis or premature degradation of the replacement valves (Hawkins et al., 2016; Mozzicato et al., 2014).

Pharmacologically, AGS poses challenges in medication selection, as alpha gal antigens may be present in various sources. Patients with AGS are at an increased risk of hypersensitivity reactions when exposed to medications containing alpha gal, such as heparin (Hawkins et al.,

2021). Other medications with inactive ingredients derived from mammalian sources can also potentially trigger AGS (Dunkman et al., 2019).

Improving healthcare providers' knowledge about AGS is crucial for enhanced patient care. Education plays a significant role in increasing awareness and understanding of AGS among healthcare professionals (Farmer et al., 2021). Implementing protocols for identifying, managing, and treating patients with AGS are necessary to reduce perioperative risks associated with the syndrome (Thomas et al., 2020).

Forming the Team

The team for this project consisted of the author, a student nurse anesthetist, who served as the primary researcher and project lead. The author received guidance and support from an advisor at the University of North Carolina at Greensboro, as well as site support via a senior Certified Registered Nurse Anesthetist (CRNA) who aided in scheduling and structuring the implementation. While the project primarily involved individual work, the collaboration with the advisor and site provided valuable insights expertise and oversight throughout the planning and execution phases ensuring the projects inherence to rigorous academic standards and best practices in research and education.

Population and Setting

The project was implemented at a 200-bed regional public teaching hospital in central North Carolina. The anesthesia department at the hospital consists of a team of CRNAs, anesthesia assistants, and anesthesiologists who collaborate to deliver anesthesia care to patients

undergoing surgical procedures. Additionally, registered nurses (RNs) care for patients in the pre and post operative setting where they assess, interview, and make interventions for patients.

Recruitment was achieved by collaborating with management to disseminate an email containing project information. A description of the study's goals and methods were provided and a link to the pre-intervention test was provided. Assurance of confidentiality of respondents was made and the test itself included an affirmative consent item. Participation was voluntary. The sample was a convenience sample of CRNAs, anesthesia assistants, and RNs at the facility. A quick response (QR) code with a link to the pre-intervention test was also available directly before the presentation.

Do: Implementation

The "Do" portion of the Plan-Do-Study-Act (PDSA) cycle implements the planned intervention or action (Moen & Norman, 2010; "Plan-Do-Study-Act, 2020). In this phase, the interventions are put into practice to be tested and measured ("PDSA: Plan-do-study-act," 2022). The goal is to observe how the implemented intervention performs in the real-world, then gathering data to evaluate the impact ("Plan-Do-Study-Act," 2020).

Intervention

The project used a pretest posttest quasi-experimental design to assess the impact of an educational session and availability of educational resources on healthcare providers' knowledge about alpha gal syndrome. Healthcare providers were recruited via e-mail with the collaboration of the department management. Identical pre and post tests were administered to determine the impact of the intervention. The test was adapted by the primary investigator from the tool

created by Farmer et al. (2021) (appendix B). Face validity was established via consultation with the project advisor.

The pretest was emailed out two weeks before the educational intervention was planned. Then, an in-person education intervention was completed. It consisted of a 15-minute multimedia presentation delivered to participants that provided comprehensive information about AGS. Covered topics included the history of ASG and how it was discovered in America, pathophysiology of reactions, triggering medications and inactive ingredients, methods to identify at risk patients, and how to manage and avoid reactions. Additionally, a reference was created that contained information about medications capable of triggering and alpha gal response in the pre, intra, and post-operative settings (appendix C). This served as a resource for healthcare providers to access information about AGS. Information was available both electronically and in printed format. A two-week wash out period was given after the education intervention, then a post-test was administered to assess the participants' knowledge retention.

Data Collection

Data was collected via multiple choice test utilizing Qualtrics software where participants completed a test with questions assessing knowledge about alpha gal syndrome (appendix B). Participant anonymity and confidentially was preserved by not collecting any identifying information such as names or contact details. Data included test responses and general demographic information. Tests were paired though the creation of a unique participant created identifier. The pairing strategy allowed for anonymous comparison of participants' results before and after intervention.

Study

The "study" portion of the Plan-Do-Study-Act (PDSA) cycle is where data that was collected in the do phase is analyzed and interpreted (“PDSA: Plan-do-study-act,” 2020). The objective was to determine if the plan resulted in improvement, if the investment was justified, what trends were identified, and what side effects were noted (“PDSA: Plan-do-study-act,” 2022). For this project, the scores from both the pre-test and post-test were analyzed to determine any statistically significant improvements. This phase allowed for a comprehensive assessment of the impact of the educational intervention on knowledge acquisition and retention.

Data analysis

Pre-test and post-test data were subjected to a paired t-test to assess the impact of the intervention in improving knowledge of alpha gal syndrome among healthcare providers. The paired t-test is useful for analyzing data from the same participant before and after an intervention allowing for a direct comparison of the mean differences. First, the mean knowledge scores for the pre-test and post-test were calculated. The paired t-test then determined whether there was a statistically significant difference in knowledge scores before and after the intervention. The null hypothesis assumed no significant change in knowledge scores while the alternative hypothesis suggested a significant improvement in knowledge scores.

Additionally, test scores were compared against demographic data including number of years of practice and type of health care degree. This comparison allowed for evaluation of potential variations in knowledge improvement based on these demographic factors. Results were held on a password protected and encrypted hard drive controlled by the PI.

Results

There were 24 participants completed the pre-test and nine completed the post-test. Participants' experience in health care ranged from one year to greater than 30 years. Participants ages ranged from 25 to 64 years. Six participants were CRNAs, eight were RNs, one was an anesthesia assistant, and five declined to report education.

Overall, pre-test scores averaged 9.4 out of a possible 11 points while overall post test scores averaged 10.4 out of 11 possible points. CRNAs averaged 9.3 points on the pre-test and RNs averaged a score of 10 points. Four CRNAs and three RNs completed the post-test. A paired t-test was completed yielding a one tailed P value of 0.055. Since $p>0.05$, the null hypothesis cannot be rejected, and it can be concluded that we do not have sufficient evidence to prove that there is a statistically significant difference in scores. None of the respondents reported caring for AGS patients in the period between the beginning and end of the study.

Discussion

The results of the study should be viewed with the purpose of the study in mind, evaluating the impact of an educational intervention and resource creation on healthcare workers' knowledge about alpha gal syndrome (AGS). Data analysis did not reveal a significant change in pre-test and post-test scores. Statistical testing suggested that the educational intervention did not lead to a significant improvement in knowledge.

However, comparing the study's findings to those of Farmer et al. (2021), who also evaluated healthcare workers' knowledge of AGS, reveals some interesting insights. In Farmer et al.'s (2021) study, participants had lower mean scores in both the pre-test and post-test. Farmer et al. saw a mean score of 5.4 on the pre-test and 8.6 on the post test, compared to this study which

saw a mean score of 9.4 on the pre-test and 10.4 on the post-test. While both studies were completed in the southeastern United States, populations were different between the two studies; this study contained CRNAs, anesthesia assistants, and RNs, while Farmer et al. focused on only RNs. The different professional backgrounds and levels of exposure to AGS patients may have influenced the baseline knowledge levels and subsequent improvements in knowledge.

Another possible explanation for the lack of significant change in scores could be that the participants in this study already had a higher-than-average baseline level of familiarity with AGS. Informally, participants reported recently caring for a patient with the syndrome and had acquired knowledge about AGS through their own research because of their prior exposure to the syndrome in patient care. The PI postulates that this accounts for some of the differences between the data in this study and that collected by Farmer et al. (2021).

Considering the translational framework of the Plan-Do-Study-Act (PDSA) cycle, it is important to note that the intervention's impact may not have been fully realized within the study period. The PDSA cycle allows for iterative improvements, and the educational intervention may require additional time or follow-up assessments to gauge its long-term effects accurately.

Act

The "Act" portion of the PDSA (Plan-Do-Study-Act) cycle focuses on what the next steps are given the results in the prior steps (“PDSA: Plan-do-study-act,” 2022). Success or failure of the plan is determined, and if it was indeed successful the plan should be used again (“PDSA: Plan-do-study-act,” 2022). If unsuccessful, it is advised to return to the “plan” step (“PDSA: Plan-do-study-act,” 2022.

The lack of significant changes in the participants' knowledge scores may suggest that educational intervention was ineffective. However, it could also be that health care providers educational needs have exceeded general information about alpha gal and become more complex. With this in mind, current research is ongoing to evaluate the feasibility of adapting current early recovery after surgery protocols to the specific needs of the patient with alpha gal syndrome. Sharing the results of this study with the group evaluating early recovery after surgery protocols could give insights into baseline knowledge of the healthcare worker about alpha gal syndrome in a local geographic region.

Limitations

Limitations to the study include sample size and characteristics. The sample size was restricted due to the availability of participants within the health care institution from which they were recruited. Small samples have intrinsic limitations and may not accurately represent the entire population of health care providers (Andrade, 2020). The data from a small sample is more susceptible to outlier variation and can lack statistical power to detect subtle effects (Andrade, 2020).

Another limitation of this study is the characteristics of the sample. The participants in the study were recruited from a single heath care institution and it is important to recognize that their level of familiarity with alpha gal syndrome may not be representative of health care providers as a whole. Furthermore, some of the participants had recently cared for patients with alpha gal syndrome which may have contributed to a higher baseline knowledge about the disease. Therefore, results lack generalizability and caution should be used when extrapolating

these findings to health care providers who have had more limited exposure to alpha gal syndrome.

Another potential limitation related to sample characteristics is volunteer bias. It may be that health care providers who volunteered to participate in the study had higher baseline knowledge of alpha gal syndrome than members of the entire population. Self-selection bias could have influenced participants with more knowledge than their peers to participate. Thus, the data comparing pre and post groups might not be generalizable to a wider population. Additionally, the focus of this project was the short-term impact of education and resource availability on health care providers' knowledge of alpha gal syndrome. Long term sustainability and improvement retention were not assessed.

Recommendations for Future Practice

The first recommendation for future practice is the integration of alerts into electronic medical record systems to alert healthcare providers about patients who may have alpha gal syndrome (AGS) and the medications that may trigger allergic reactions. By incorporating AGS specific alerts into the electronic medical record, healthcare providers can receive real-time information and reminders about AGS patients under their care. These alerts can help facilitate early identification of AGS cases, ensure appropriate medication selection, and prompt providers to consider alternative options when choosing medications. The integration of AGS alerts into the electronic medical record system would improve patient safety, reduce the risk of adverse reactions, and help standardize care for individuals with AGS.

The second recommendation is for pharmacy departments to create and maintain a list of medications with both active and inactive ingredients that can potentially trigger alpha gal

syndrome. While active ingredients are typically easier to identify as triggers, the inclusion of inactive ingredients in this list is crucial due to their potential to contain alpha gal antigens. By maintaining this medication list, pharmacies can play a vital role in assisting healthcare providers to make informed decisions when administering medications to patients with AGS, ultimately reducing the risk of adverse reactions. Additionally, making this information available to patients equips them to be vigilant when purchasing over-the-counter medications and ensures they are aware of potential triggers associated with AGS.

Alongside healthcare professionals, patients with AGS should be provided with comprehensive education and support. Patient education materials should be developed to improve their understanding of AGS, dietary restrictions, potential triggers, and emergency action plans. Support groups and online communities can also be established to facilitate peer support and knowledge sharing among individuals with AGS.

Conclusion

In conclusion, this study aimed to assess the impact of an educational intervention and resource creation on health care workers' knowledge about alpha gal syndrome (AGS). Alpha gal syndrome (AGS) is a hypersensitivity reaction triggered by mammalian products and acquired from the bite of the lone star tick. Medications and medical devices can trigger reactions in impacted people. In contrast to the literature, this study found good baseline knowledge about alpha gal syndrome and no significant changes in knowledge scores before and after intervention. This might be explained by health care providers seeing AGS in clinical practice more frequently and educating themselves on the disease.

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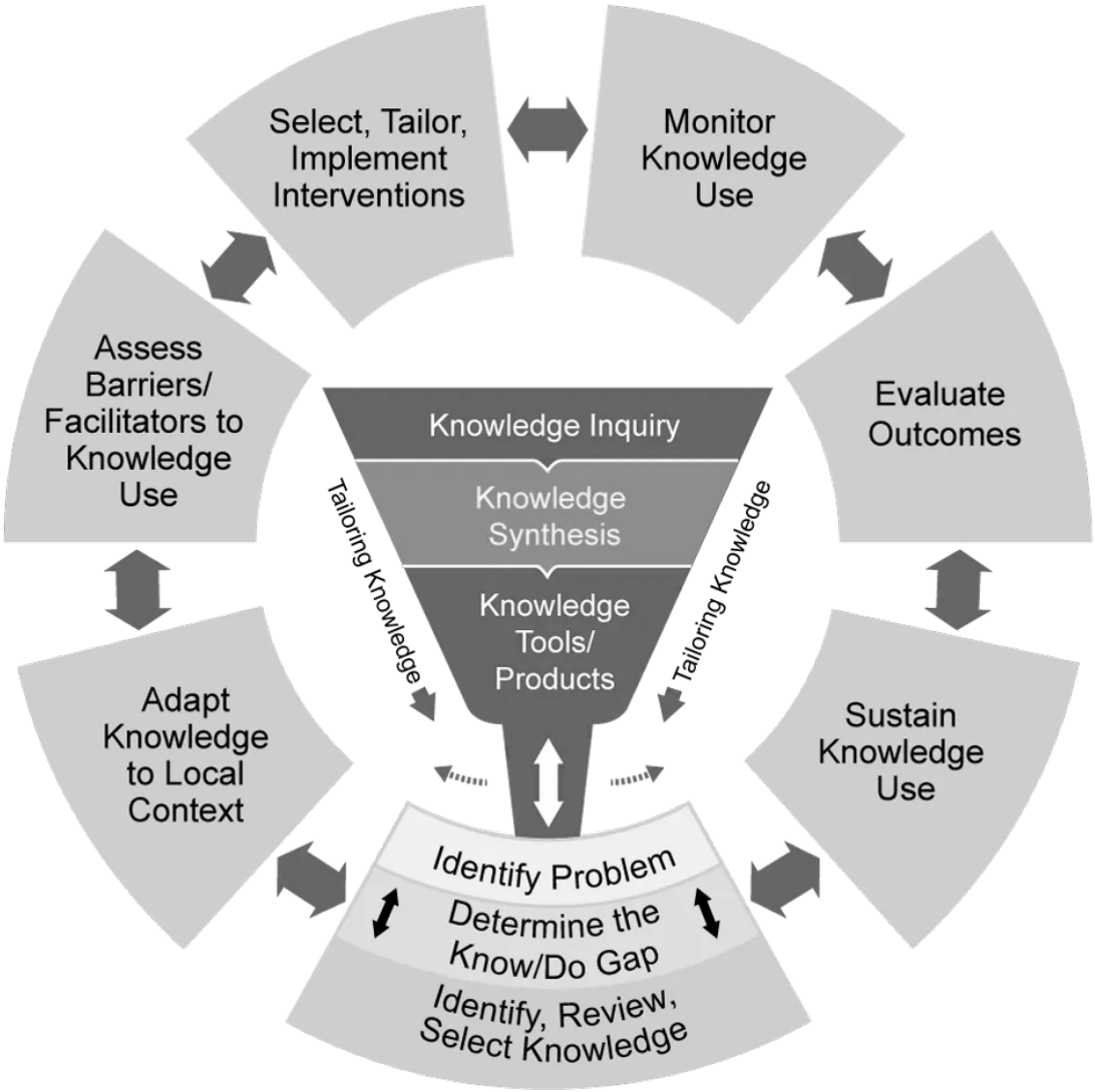
Appendix A

Knowledge to action process (Graham et al., 2006).



Appendix B
Test Questions

1. How is alpha-gal sensitivity transmitted to humans?
    1. Contaminated water
    2. Tick bite
    3. Improperly cooked meat
    4. Bee sting

2. How long after oral ingestion do symptoms typically appear?
    1. 30 seconds
    2. 1 to 2 hours
    3. 3 to 6 hours
    4. 12 hours

3. What food elicits an allergic reaction in patients with Alpha gal syndrome?
    1. Red meat
    2. Toxins
    3. Wheat containing foods
    4. Tree nuts

4. What's alpha-gal?
    1. Protein
    2. Fat
    3. Vitamin
    4. Carbohydrate

5. What diagnostic work does the provider order to screen for Alpha gal syndrome?
    1. Complete blood count
    2. Basic metabolic panel
    3. IgE antibodies
    4. Chest x ray

6. What symptoms can a patient present with during a reaction?
    1. Itching on palms of hands and soles of feet
    2. Urticaria
    3. GI pain
    4. All of the above

7. What medications can be used to treat an acute alpha gal reaction?
    1. Diphenhydramine
    2. Epinephrine
    3. Inoculation
    4. Both 1 and 2 are correct

8. True or false: alpha gal syndrome can be life threatening:
    1. True
    2. False

9. What medication could potentially elicit an allergic response in a patient with Alpha gal syndrome?
    1. Heparin
    2. Enoxaparin
    3. Hydromorphone
    4. Both 1 and 3

10. What's the most important task for nurses regarding patients with Alpha gal syndrome?
    1. Review laboratory results
    2. Obtain a detailed history
    3. Physical assessment
    4. Assess motor deficits

11. What patient history finding indicates a patient is at risk for undiagnosed alpha gal syndrome?
    1. International travel in the last 90 days
    2. Autoimmune disease like rheumatoid arthritis
    3. Hypoalbuminemia
    4. Allergy to red meat

12. What is your educational background?
    1. Anesthesia assistant
    2. CRNA
    3. Anesthesiologist
    4. Prefer not to answer

Appendix C

Medications capable of triggering alpha gal reactions with inactive ingredient listed

Medication name	Inactive ingredient
Acetaminophen liquid	Glycerin
Acetaminophen tablets	Magnesium stearate
Alvimopan	Gelatin
Aprepitant	Gelatin
Celecoxib	Gelatin
Gabapentin capsules	Gelatin
Haloperidol injection	Lactic acid
Heparin (Porcine derived)	Pork
Hydromorphone injection	Lactic acid
Ibuprofen suspension	Glycerin
Lidocaine patch	Gelatin
Methadone solution	Glycerin
Oxycodone tablet	Oxycodone tablet
OxyContin	Magnesium stearate
Pregabalin	Gelatin
Surgifoam powder	Gelatin