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Prophylaxis of Food Allergen Sensitivity By Dustin Gottfeld PAL 5660 - Publication elective R6 Due 7/5/2020

<u>Introduction</u>

The incidence of food allergies has been rising, now nearing 10% prevalence in the developed world. The rapid rise has so far been unexplained. These allergies are usually IgE mediated and can often cause life-threatening effects that can affect an individual for the rest of their lives. These food allergies can have a severe and drastic effect on a person's lifestyle. Food allergy prevention can help to ensure others do not have to live with this burden. [1,2]

The Hygiene Hypothesis and Dual-Allergen Hypothesis are differing explanations for the development of food allergies, and most of the evidence has focused on peanut allergies. These two hypotheses suggest different methods for prevention of peanut allergies among infants. It is important to determine the application of which hypothesis will better help prevent the development of food allergies. [1,3,4]

The Hygiene Hypothesis has changed throughout the years to evolve beyond the assumption that it is pathogenic microorganisms that help protect an infant from developing allergic disease. The theory now focuses on the belief that it is the diversity of a child's microbiota that creates a beneficial balance of microorganisms which can help prevent the development of allergic disease. The microorganisms that inhabit individuals with allergic diseases has also been shown to differ greatly from those without allergies. A restoration of healthy microbiota may help prevent the development of allergies in those whose microorganisms are unbalanced. Some bacteria that have been identified as beneficial are found in breastmilk: Lactobacilli and Staphyloccocus aureus. These organisms may help educate the evolving immune system. [1,3,4,5,6,7]

Alternatively, the Dual-Allergen Hypothesis states that early environmental exposure to an allergen through the skin can create sensitivity within an infant, thus leading to a food allergy. Studies have shown that this may be prevented by introducing the allergen orally before the infant is exposed environmentally. For instance, administering oral peanut allergens at 6 months, but not before 4 months of age, has been shown to be effective in preventing the development of peanut food allergies. [4,8,9,10]

There is a gap in the current medical knowledge on this subject. It is important to determine whether an infant's microbiome should be diversified (per the Hygiene Hypothesis), if an infant should be orally administered peanuts at an early age (application of the Dual-Allergen Hypothesis), or if both preventive techniques should be applied.

I will determine which allergy hypothesis should be applied for preventive techniques in infants, or if both methods are appropriate to be done concurrently, with a specific focus on peanut allergies. I will conclude whether it is the best practice to administer probiotics to infants, peanut protein at 6 months old, or both.

Methods and Results

Currently, providers decide on a case-by-case basis which hypothesis they want to employ for allergic disease prevention. Some providers do not utilize any food allergy prevention methods or use

experimental immunotherapy techniques, but research shows that both methods described in this paper show promising results. I believe both approaches have merit and can be applied concurrently to ensure the pediatric population has adequate and optimized food allergy prophylaxis. [4,5,8,11,12]

Due to the safety of probiotic administration in pediatric patients, it would be logical to make administration of probiotics to all immunocompetent 6 month old infants a routine practice. This would result in minimal adverse effects with an increased likelihood of food allergy prophylaxis. In addition to probiotic administration, oral tolerance induction with peanuts in 6 month old infants can also be a safe practice if parents are well educated regarding when and how to administer peanut butter to their infant. Parents must also be well educated about the signs of anaphylaxis and steps to take if the infant shows signs of any degree of allergic reaction. [3,4,6,7,8,9,10,13]

Both hypotheses describe different causes for allergen sensitization. Therefore if both theories are applied for food allergy prevention, the risk of developing these allergies can be greatly reduced. The new standardized practice for prophylaxis of food allergen sensitivity should include early probiotic administration and oral peanut tolerance induction, both at approximately 6 months of age.

Conclusion

As of now, there are no specific guidelines for the best method for food allergy, specifically peanut allergy, prophylaxis. There are two separate hypotheses that can be applied to infants that have been shown to prevent the development of peanut allergies. While these hypotheses and their application are different, they are not mutually exclusive and can be performed concurrently. [4,5,8,11]

The Hygiene Hypothesis states that the development of allergies can be the result of an imbalance in the quantity and/or diversity of beneficial gut microorganisms. The application of this hypothesis in food allergy prevention includes methods of restoring or providing normal gut flora to the patient. Alternatively, the Dual-Allergen Hypothesis states that food allergies can develop if a patient is environmentally exposed to an allergen (often through the skin) prior to oral introduction of the same allergen. The application of this hypothesis in food allergy prophylaxis includes oral tolerance induction, which is the oral administration of the allergen prior to environmental exposure. [1,3,4,5,6,7,8,9,10]

There has not been previous research comparing these hypotheses or methods. It was surprising to find that both of these methods show promise. Their relatively safe application in infants and the fact they are not mutually exclusive supports their use together as best practice guidelines for peanut allergy prophylaxis.

According to Özdemir, the best application of the Hygiene Hypothesis in allergy prevention is the administration of probiotics, particularly Bifidobacterium and Lactobacillus. Both of these strains are present in yogurt and cheeses. Since yogurt is relatively safe when administered to infants and contains the strains necessary to establish healthy gut flora in the patient, the best Hygiene Hypothesis method for peanut allergy prevention is to administer yogurt to infants. Administration of yogurt would ideally begin between 6-12 months of age. The specific quantity for administration has not been sufficiently studied, but should depend on how the infant tolerates the yogurt. Further study needs to be performed to determine minimum effective probiotic dosing to establish necessary healthy gut flora. Nowadays, baby formula can contain microorganisms tailored to mimic breast milk, including the organisms Bifidobacterium and Lactobacillus. Because of this, an alternative application of the Hygiene Hypothesis can be the administration of baby formula containing these probiotic strains. Yogurt,

however, is better researched and significantly cheaper than tailored baby formula and can be administered in conjunction with breastmilk, which has shown to have a variety of other positive health effects when compared to exclusive formula feeding. [1,3,5,6,7,10,14]

According to Greer, the best application of the Dual-Allergen Hypothesis for peanut allergy prophylaxis is oral tolerance induction via the administration of peanut protein. The study indicated that consumption of 2 grams of peanut protein per week beginning at 6 months old lowered the prevalence of peanut allergies. Therefore, the best Dual-Allergen Hypothesis method for the prevention of peanut allergies is to administer 2 grams of peanut butter every week starting at 6 months old. If oral tolerance induction is performed prior to a patient's environmental exposure to the antigen, the administration of peanut protein is relatively safe. It is important to initially administer a small quantity only and thoroughly monitor the patient after the infant is given peanut butter the first two times to ensure anaphylaxis does not occur. To ensure the safety of the infant, the first two administrations can be performed under clinical observation and should only continue if the patient can tolerate it. If this is not possible, the parent or guardian should be educated about the signs and symptoms of the different levels of allergic reactions and how to identify if the infant needs to be taken to the emergency department. If these safety measures are followed and peanut administration is halted after an allergic reaction is identified, administration of peanut protein to infants is relatively safe. [4,8,9,10,12,15]

Due to the low risks associated with the safe administration of both probiotics and peanut protein at 6 months old, I believe the best and most prudent course of action is to apply both of the two prevailing hypotheses to prevent peanut allergy development. The best practice would include advising parents to give all healthy and immunocompetent infants yogurt containing Bifidobacterium and Lactobacillus, in addition to 2 grams of peanut butter every week beginning at 6 months old.

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