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The Potential use of Genetic Screening on Infants to Identify High Risk Individuals and Limit the Development of Peanut Allergy

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Abstract

Peanut allergy is one of the most life-threatening food allergies that can have a dramatic effect on quality of life, so as to provoke fatal reactions.Importantly, symptoms can occur following exposure to only very tiny amounts of peanut protein. Findings show that peanut allergy has genetic influence rather than mere chance. There are solutions that only focus on ways to alter the allergic patient's immune system to peanut. However, with the advent of genetic screening, novel strategies can be proposed to solve the problem of peanut allergy from the source. This paper aims to outline the characteristics of peanut allergy, how anaphylaxis occurs, ways in which the quality of life of patients with peanut allergy is affected and the importance of limiting the development of peanut allergies with the use of genetic screening.Research findings show that genetic screening in infancy can be imperative in identifying individuals with a high risk of peanut anaphylaxis and also in limiting the development of peanut allergies.

Keywords: genetic screening, genetic test, peanut allergy, anaphylaxis, genes, quality of life

Introduction

Genetic screening plays an important role in modern medicine. There are several types of genetic screening: prenatal, newborn, susceptibility and forensic among others. For the newborn disorders, which are hardly identified during infancy, newborn genetic screening comes in handy. It is a simple method that requiresbloodsample, tissue, hair piece, amniotic fluid from placenta for analysis. It is afterwards sent for analysis, which identifies abnormalities that can cause a serious effect. Newborn genetic screening has been used in the identification of disorders such as phenylketonuria and sickle cell disease among many others at infancy. Early identification helps in early intervention and planning for the care of patients. Furthermore,food allergies have become common in modern times. There is no known treatment of food allergies and its prevalence constitutes more than 1.0 percent of the population of the United States alone(Gupta et al., 2019). Peanut allergy deserves particular attention. Peanut allergy in infants constitutes 0.6 percent of the general population (Gupta et al., 2019). In addition, Al-Muhsen and colleagues (2003) followed a cohort study on the Isle of Wight from birth until the age of 4 years. The participants were asked about their allergic reactions; skin prick tests were performed on them and their peanut specific IgE was measured. At age 4, 1.1 percent of the 1218 children were sensitized to peanuts, and 0.5 percent had an allergic reaction to peanuts. An additional 1.2 percent of children were sensitized to tree nuts, with 0.2percent having experienced an allergic reaction. On the basis of this and other studies that have reported similar prevalence (Gupta et al., 2019, Grundy et al., 2002) the estimated prevalence of peanut allergy in developed countries is between 0.6% and 1.0%. Recently, a follow-up study (Grundy et al., 2002) demonstrated that the prevalence of peanut allergy had increased to 1.5% on the Isle of Wight, which suggests that the problem is growing. This is a huge burden considering that the allergy is a life-long condition

with episodes that are life-threatening. Recent efforts to manage peanut allergies have been futile.Chu et al. (2019)posit that drugs that have been used to desensitize individuals against the allergic effect of peanut have three times the probability of causing an allergy that the drug is supposed to prevent. Epidemiological studies on peanut allergies in genetics using monozygotic twins have shown higher concordance rates implying that peanut allergies are genetic(Chu et al., 2019). It is on this background of previous research findings it can be concluded that genetic screening is crucial on newborns in order to limit new developments of allergies, in particular peanut.

Anaphylaxis

Anaphylactic reaction

Anaphylaxis is a systemic reaction involving multiple organ systems (Peavy & Metcalfe, 2008). It is usually associated with exposure to allergens and the release of mediators from mast cells and basophils(Peavy & Metcalfe, 2008). Anaphylaxis may potentially lead to death, although this is not the usual outcome (Peavy & Metcalfe, 2008). The sudden and often unanticipated onset and the catastrophic physiological impact of anaphylaxis make proper diagnosis and appropriate treatment critical for beneficial outcomes. As described by Portier and Richet (2019), anaphylaxis has been recognized as both a dangerous and a puzzling disease.

Events in Anaphylaxis

Anaphylaxis, for the most part, is believed to arise from the activation of mast cells and basophils through a mechanism generally understood to involve crosslinking of immunoglobulin (Ig) E and aggregation of the high-affinity receptors for IgE, FcεRI (Peavy & Metcalf, 2008). Upon activation, mast cells and/or basophils quickly release preformed mediators from secretory granules that include histamine, tryptase, carboxypeptidase A, and proteoglycans. (Martha,

1990). Downstream activation of phospholipase A2 (PLA2), followed by cyclooxygenases and lipoxygenases, produces arachidonic acid metabolites, including prostaglandins, leukotrienes, and platelet activating factor (PAF). (Peavy & Metcalf, 2008). The inflammatory cytokine, tumor necrosis factor-α (TNF-α) is released as a preformed mediator, and also as a late-phase mediator with other cytokines and chemokines (Peavy & Metcalf, 2008). Histamine stimulates vasodilation, and increases vascular permeability, heart rate, cardiac contraction, and glandular secretion (Martha, 1990). Leukotrienes produce bronchoconstriction, increase vascular permeability, and promote airway remodeling (Martha, 1990). TNF-α activates neutrophils, recruits other effector cells, and enhances chemokine synthesis (Ogawa, 2017). These physiological effects contribute to the overall pathophysiology of anaphylaxis that variably presents with respiratory and cardiovascular symptoms, nausea, cramping, and other gastrointestinal symptoms.

Peanut Allergy and Genes

While there are many types of food allergies, peanut allergy is particularly troublesome, for a number of reasons. Most importantly, peanut allergy usuallyleads to more serious reactions than other allergies including death. In addition, currently there is only one successful “treatment” which is to completely avoid peanuts. Importantly, symptoms can occur following exposure to only very tiny amounts of peanut protein. One peanut contains about 200 mg of protein (Goldam,1998).In fact, people mostly develop symptoms just after a small exposure to peanut. A study designed to determine the minimum dose of peanut protein capable of eliciting an allergic reaction in highly sensitized individuals, subjective symptoms were reported with doses as low as 100 µg, and objective signs were evident at 2 mg (Hourihane et al., 1997). Peanut allergy is defined as reacting within 60 minutes after ingesting either peanut or other products with peanut

as an ingredient(Gupta et al., 2019).It was found that the active molecules in the peanut are evenly distributed through the entire peanut which were named as Ara h 1 that interacted with IgE epitopes (Wichers, de Beijer, Savelkoul, & van Amerongen,2004).Besides, it has been debated whether peanut allergy is animmunological, genetic or if it is environmental influence that people develop over time. There are all indicators that peanut allergy is a phenotypic reaction with influence coming from the genes. This was shown by the epidemiological studies that have been done to link the peanut allergy to genetics (Fiocchi &Ebisawa, 2018). These studies have employed the use of monozygotic and dizygotic twins to link the possibility of food allergy to genes. In one of the studies, Sicherer et al., (2000) recruited monozygotic and dizygotic twins and exposed them to the same amount of peanut. The study assumed that monozygotic twins share a common gene while dizygotic twins do not. The results established that monozygotic twins had a higher pairwise concordance rate of 64.3 % of peanut allergy compared to dizygotic twins who had 6.8 %. The finding is a pointer that the allergy has genetic influence rather than mere chance. It is a finding that has prompted laboratory research to establish the link using the gene marker of the allergies. In addition,Glaumann, Nopp, Johansson, Borres, & Nilsson, (2013) scanned more than 8000 Canadians with peanut allergy against those without the allergy and seems there is a link between gene c11orf30/EMSY(EMSY) with a peanut allergy. Individual with c11orf30/EMSY(EMSY gene have higher chances of reaction when earlier sensitized by peanut allergens (Brough and Kull,2018). This gene is implicated in many other allergies which included but not limited to eczema, allergic rhinitis, and asthma. It is currently highly linked with food allergies and any other reactions that develop. The finding is important in diagnostic, preventive and curative purposes. The knowledge of the disease to genetic levels opens avenues of genetic screening and management.

Impact of food allergies on quality of life

There was a study done that analyzed the impact of food allergy on quality of life (HRQL) in adults and children in different countries. Julie and colleagues (2019), reported that patients with food allergies have a significant poorer quality of life compared with patients with diabetes. 367 peanut allergy (PA) subjects and 442 parents/caregivers completed a baseline assessment. (Julie et al., 2019) .The Worse PA-related QoL was seen with increasing age (4-6yo, 7-12yo, teens) across allFood Allergy QoL Questionnaire (FAQLQ) domains reported by parents/caregivers and on 2 of 3 domains reported by subjects (8-12yo, 13-17yo, adults). The Emotional Impact (EI) domain had the highest score among subjects (4.80), followed by Allergen Avoidance and Dietary Restrictions (4.40) and Risk of Accidental Exposure (4.20) (Julie et al., 2019).In contrast, Food Anxiety (4.23) had the highest score among parents/caregivers, followed by Social and Dietary Limitations (4.17) and EI (3.82)(Julie et al., 2019).Differences in score patterns by demographic and disease history variables were also seen.(Julie et al., 2019)

Genetic Screening

Identification

It is important to find the connection between peanut allergy and the newborn. Using genetic screening this is done before the infants' exposure to an actual peanut. Finding the locus of the gene responsible for peanut allergy, c11orf30/EMSY(EMSY), can be done at birth and medical advice is given on how to manage the condition and avoid misdiagnosis. Howell et al., (1998) established that the human race has 8000 diseases where one such allergies are diagnosed after several misdiagnoses. It may be hard to come with an outright and accurate diagnosis when it comes to allergies since food share similarities. Many products and food items are made of peanut and therefore expose children to unprecedented allergies(Glaumann et al., 2013). This

includes perfumes, skin oil and food product such as peanut butter. The first exposure may not have reactions and therefore parents may fail to associate the allergy with peanut when they expose their children to peanut(Sicherer et al., 2000). To that effect, the suspicion index may be low and most of the parents think it is just a disease like any other. Telling the history of the disease in the hospital may not capture details that are close to peanut allergies. The negative effect is the delayed diagnosis, the suffering of the patients and deaths (Allyse& Wick, 2018). The genetic screening, therefore, makes it easy for the physicians to identify infants with allergies and plan for the management and how to avoid exposure to the allergen(Brough & Lack, 2018). This will reduce the suffering that can go unknown for a long time, for both the patient and his/her family. This is especially important because people may be allergic to multiple allergens which can significantly impact their quality of life.

Limiting Development of Peanut Allergies

Genetic screening has been used in limiting the development of undesired diseases since late twentieth century. Diseases such as sickle cell, phenylketonuria, and cystic fibrosis have been effectively limited through genetic screening(Brough & Lack, 2018). However, it should be appreciated that there is no repair that can be made externally to limit the development but rather through a combined approach such as identifying the sex-linked, the autosomal recessive and dominant genes then working on the probability of it recurring(Adamson, 2019). Another approach is through in vitro fertilization where only the ova and sperm that are free of genetic errors are used in the fertilization rather than natural and random fertilization that presents an equal chance for either combination of gene thus resulting in genetic errors and the diseases(Adamson, 2019). Therefore, the task that has to be accomplished is a complete definition of the locus of the gene that determines food allergies such as peanut(Roy, Mao,

Huang, & Leong, 1999). This description will help in genetic counseling, the in vitro fertilization and development of drugs that have genetic signaling to reduce the release of proteins that cause allergies (Roberts and Dotson, 2018). Through this approach, it is possible to limit the development of peanut allergies at the prenatal stage and also in the development of therapeutic agents that target the gene.So far immunological medicine has been the mainstay for the management of the peanut allergy.Glaumann et al., (2013) predicated that the immunological therapydesensitizes individual with the allergy from the allergen in the peanut. However, there have been complaints about the drug as some developed allergic-like reactions after using the very drug that is supposed to prevent the reaction when compared with those that got the placebo(Chu et al., 2019). This finding further indicates the need to research the best approach with little or no side effect such as genetic screening and genetic-based therapeutic agents.

Benefits of Genetic Screening

There are several benefits of genetic screening, however, the most important one is the sense of relief from uncertainty.The relief from uncertainty is very important no matter what the end result might be. When the unborn child has a proper diagnosis, the appropriate treatment can be given on time and it will have a better chance of living longer. This ensures that regular check-ups are done, and all measures are taken to minimize the risk. Inaddition, the results of a genetic test can provide useful information when planning for future children. If someone in your close family has allergies it is always safer to test the unborn child during pregnancy just to make sure you are aware of things that might potentially harm the baby's life. This gives the parents the opportunities to be prepared both mentally and financially. Since genetic conditions are passed down onto the next generations it will be useful for other family members as well which prevents from being misdiagnosed.

Conclusion

In conclusion, the prevalence of peanut allergy and the fact that it is a lifelong condition warrants research in this field especially to the genetic level because that is where all the human health conditions lie. The current knowledge of peanut allergies is limited to the epidemiological studies that have linked it to genes using monozygotic and dizygotic twins (Chu et al., 2019). Laboratory studies on the subject with and without the peanut allergies have established the likely gene that is associated with the peanut allergies (Du Toit and Sayre, 2018). The limitation on this subject is that the current knowledge is not sufficient enough to establish genetically targeted agents fully employing genetic screening to limit the development of this disorder as done in other conditions such as sickle cell disease.With the advance of technology, the contributions of genetic factors still need to be clarified. However, a lot more studies with large sample size and improved phenotyping are needed to ensure best results. The future possibilities of such testing lie in further research dissecting the complex interplay between genetic components and diverse environmental factors, including the microbiota, in the pathogenesis and expression of food allergy. In the near future, it would be of a huge benefit if a panel of biomarkers to identify high-risk populations are established, where preventive measures can reduce severe food allergy emergencies, facilitate accurate identification of allergen sources and predict effective treatment options and thus improve overall patient care.

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