Diets and Immunotherapy

Subjects: Others

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Maternal diet has significant effects on development of childhood atopic disease and hypersensitivity development. However, the gestational dysfunctions demanding special diets and mothers' habitual diets is becoming a widespread phenomenon. Adherence to these diets is mandatory in most cases; however, their immunological implications can be manifested in the profile of identified antibodies in the serum of children. Epigenetic modulation appear to be one of the most promising immunotherapy method. Especially methylation may serve as an anchor upon which gene expression modulates reaction severity, but depending on the gene, both increased and reduced methylation can be a factor in the induction of an allergic process and its severity.

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1. Introduction

The human immune system is immensely complex but is not always able to develop tolerance to food allergens. The drawback of developing an immune system that may recognize and respond to infections is the potential for hypersensitivity reactions. These manifest as allergic responses to environmental agents among others. Despite the intensive advancement of knowledge in the area of aetiology and progression of allergic disease, this problem affects an increasing number of people [1].

2. Food Allergy

According to the World Health Organization, it is currently the third most commonly diagnosed chronic disease and food allergy rates are now higher than ever before. According to the European Academy of Allergy and Clinical Immunology (EAACI), more than 150 million Europeans suffer from chronic allergic diseases as per the current scenario and half of the entire EU population is foreseen to be affected by 2025 [2]. It has been estimated that the immune system of about half of newborns is not able to develop tolerance to food-origin proteins [3]. The global food allergy diagnostics and therapeutics market size was valued at 2.69 billion USD in 2018 and is expected to grow by 7.4% over the next 10 years, whereas the global allergy immunotherapies market is expected to reach 3.63 billion USD by the end of 2025, growing by 10.8% during 2019–2025 [4]. According to a report published in 2018 based on children less than 5 years old, the prevalence of challenge-proven food allergy has been reported to be 4% in the UK, 3.6% in Denmark, 6.8% in Norway [3], and in Poland in 2016, it was 8% [5]. The discrepancies

and underestimation in those results are always difficult to interpret, given that allergies can be manifested immediately but can also give a delayed reaction.

The consequence of the progression of allergic diseases including food allergy is a number of possible health complications and the well characterised allergic march as a consequence of skin and epithelial barrier dysfunction [6][7]. However, the latest research mainly focuses on demonstrating possible links between allergic diseases and the development of subsequent eating disorders, psychosocial drawback [8], and inflammatory autoimmune diseases with humoral regulation [9]. Some of those diseases, because of commonalities in terms of susceptibility loci, genetic pathways, and genomic regulatory sites, may also explain the dramatic increase in the coincidence of mentioned disorders that are highly heritable.

3. Immunotherapy

Properly selected immunotherapy plays an important role and might be conducted through induction, enhancement or suppression of an immune response on different levels, including gene expression and its epigenetic activity modulation [10][11] One of the most promising types of therapy is based on nutrigenomics. The role of foetal programming in the prevention and therapy of various inflammatory and atopic diseases are also the widely discussed randomized controlled trials on the influence of dietary intervention on epigenetic mechanisms in children who suffered from cow's milk allergy that have already done [12]Maternal dietary patterns may prevent or reduce hypersensitivity with significant reduction especially in IgG-mediated diseases [13]. A successful protocol for IgE-mediated reactions still remains a challenge, but there have been several studies published describing correlations between maternal dietary components that works preventively through epigenetic activation of mechanisms against asthma, wheezing and allergic rhinitis [14]. Nevertheless, over the last 10 years, based on retrospective studies and precise maternal and children diet and lifestyle analyses, an earlier and a more severe failure of oral tolerance during the first year of life and the likelihood of outgrowing food allergies decreased, whereas the severity of diseases increased [12][15][16]. That forces changes in the approach to conducting therapy and stimulation to analyses of factors inducing the foetal immune system in prenatal time.

Diet remains one of the dominant environmental factors that has an influence on the immune system development and function and, thus, it affects many aspects of health and disease risk [17]. Some meta-analyses of data showed that maternal probiotic and fish oil supplementation may reduce risk of eczema and allergic sensitization to food, but at the same time, emphasized that the risk of bias was high (from 25–48%) in tested studies [18]. Based on that meta-data analysis, it was found that results regarding other gestational dietary exposures, including prebiotic supplements, maternal allergenic food avoidance, and vitamin, mineral, fruit, and vegetable intake, were inconclusive or inconsistent.

Not only was the role of gestation but also preconception diet studied in infant immune system programming. There are cohort studies describing the influence of pre-conception intake of certain food groups, such as meat- or plant-based food and, except the positive impact mentioned above, it has been stated that pre-conception increased meat intake may increase the risk of wheezing, allergic rhinitis and atopic dermatitis in children [14]. However, it has

been also mentioned that the limitation might have been the use of self-reported food frequency questionnaires (FFQs) to assess food intake, possibly leading to errors caused by subject memory bias. Another study, dedicated to maternal pre-conception food intake, such as low and high fat dairy, fresh fruit, saturated and unsaturated spreads, and take-away foods, revealed some protective impact for several atopic diseases but at the same time poultry and fruit juice were adversely associated with eczema, current wheeze and rhinitis classified as “each allergy” [19]. That study was also limited by FFQs and maternal group characteristic showing that almost 30% were obese and 50% were asthmatic. Nevertheless, those studies allowed us to observe some trends: firstly, in the studied issue of the effect of various dietary components for allergy or tolerance development and, secondly, the current way of conducting such research. Most of the studies were focused on the role of a single product or ingredient in pre-conception or gestational diet, not the dietetic pattern driven by health dysfunction appearing during pregnancy. The most common gestational dysfunctions are gestational diabetes and cholestasis. Both usually disappear after childbirth but during pregnancy requires special diet. Also, the gestational vegan/vegetarian diet was tested here. Those diets were declared to be implemented because of the parental high body mass or hyperglycaemia. Finally, the gestational elimination diet was studied in this manuscript. This diet was declared by mothers with their positive history of allergy/intolerance. It was considered to be preventive and assumed an elimination of strong allergens such as milk, wheat, and nuts. In general, there is a limited number of studies evaluating the influence of gestational special diets, such as diabetic, cholestatic or elimination diets, on the specific E antibodies profile in serum of offspring. The vast majority of studies are based on surveys and self-reported manifestations of allergy and other atopic diseases, like asthma, atopic dermatitis or rhinitis, in children [20]. Clinical confirmation of the presence of antibodies and immunological parameters is especially necessary, because some people may be asymptomatic while others will suffer, e.g., as a result of a somatic reaction without immune changes.

Few studies have considered the impact of offspring, not maternal, diabetic diet on atopy prevalence in children [[21]. A significantly increased incidence of atopy was explained by lesser diversity of diet. Nwaru also emphasized that the study was focused on the group of subjects with type I diabetes in a Finnish population. Children recruited in that study carried genetic HLA-conferred susceptibility for type 1 diabetes, and they emerged from the cohort. In these studies, HLA-DQB1 was considered to be a genetic susceptibility loci not only for type 1 diabetes mellitus but also for allergic sensitization, which might have been the reason for higher correlation of all the tested variables. Another tested type of health-driven diet was allergens’ elimination [22][23][24]. Several studies have investigated the impact of elimination diet on the frequency of allergy in offspring; most of these studies have not supported the protective effect of maternal exclusion (including the exclusion of cow’s milk, eggs, and peanuts), but some of them have reported mild preventive action on cross-reactions. The immunological system developement can be also imbalanced through the reduced consumption of natural sources of not only cofactors and methyl donors, such as vitamin B6, B12, folic acid, and betaine, but also omega-3 fatty acids that can alter the methylation of *de novo* genes *in utero.* A previous study reported that maternal nutrition and the intake of these components play a critical role in DNA methylation *in utero* and the development of the offspring’s immune system in the course of many diseases [25]. Especially methylation may serve as an anchor upon which gene expression modulates reaction severity, but depending on the gene, both increased and reduced methylation can be a factor in the induction of an

allergic process and its severity. Differential DNA methylation were found to be associated with the process of peanut allergy development and severity regulation. NF-κB and its inhibitor alpha (*NFKBIA*) seem to play an important role here. The modulated gene expresion in a course of peanut allergy and severity was involwed in humoral response, chemotaxis, and regulation of macroautophagy [26].The effect of dietary components on mechanisms at the level of epigenetic variability may be an ideal method of immunotherapy.

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