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Recent advances in the management of allergy associated diseases in children

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Abstract. – The allergy symptoms could arise from variable organ systems and have fluctuating nature in severity as well as symptoms. Moreover, these symptoms could be related to multiple pathological states like common cold, chronic obstipation, diarrhea, etc. On the other hand, food allergy diagnosis that usually spread by IgE-mediated inhalant also poses a great challenge in front of the scientific fraternity. So far, many advances in the field of allergy diagnosis, as well as therapeutics, have been made. These advances include skin prick testing (SPT), serum specific IgE (sIgE) level test, component resolved diagnosis (CRD) test, etc. The present review article would be focused on important pathological states associated with allergy observed commonly in children. Moreover, tjelatest developments about timely management and accurate diagnosis are also discussed.

Key Words:
Allergy, Infants, IgE, Component resolved diagnosis (CRD), Diagnostic advances.

Introduction

The hypersensitivity reactions to a particular allergen (molecule capable of triggering an immune response) followed by antibody IgE-mediated or cell-mediated immunological mechanisms are covered under single term 'allergy'. In the last few decades, allergy associated diseases like allergic rhinitis, asthma, food allergy, etc. are on a high-rise in young infants. The allergic rhinitis is the prime initiator of allergy reports in children[1]. At present, half of the western world population is sensitized to one or more allergens[2]. Moreover, allergy associated diseases and incidences of sensitizations are continuously elevating worldwide[3,4].

The timely diagnosis of allergy is essential for treatment control, especially in young infants. So, specific and efficient diagnostic avenues are the need of hours. Studies are being conducted for the search of better test or combination of tests that provide the highest Positive Predictive Value PPV [together with a low Negative Predictive Value (NPV)]. Moreover, researchers are also exploring immune profiles of the patients with false positive results. The possible key factors responsible for allergic trigger are micro biome, endocrine disrupters, overweight, dyslipidemia, genetic factors, etc. Other possible explanations favored non- specific triggers like environment factors or food-induced reactions. The present article would review all-important developments and updates in diagnosis of allergic pathology in young infants.

Basic Mechanism of Allergy

The entrance of the allergen into the body appoints the basic molecular mechanism of allergy[5]. This is followed by absorption of the allergen by an antigen-presenting cell. The antigen is then targeted to the nearest lymph node in order to activate specific T cells. These T cells then stimulate concerned B cells by their respective differentiation to Th2 cells. The activated B cells in turn differentiate into plasma cells, which actively synthesize antibodies of the IgE isotype. These antibodies finally get bound to mast- and basophil cells for future allergic responses. So, whenever the allergen re-enters the body at a later time, these mast as well as basophil cells result allergic inflammation symptoms. Another mediator is IL-4, responsible for the differential of B cells to differentiate into plasma cells (Figure 1).

Important Allergy-Associated Pathological States and Their Management Updates

Food Allergy and its Management

Food allergy is one of the most prominent public health problem especially in children. The main player for this extensive spread is absence

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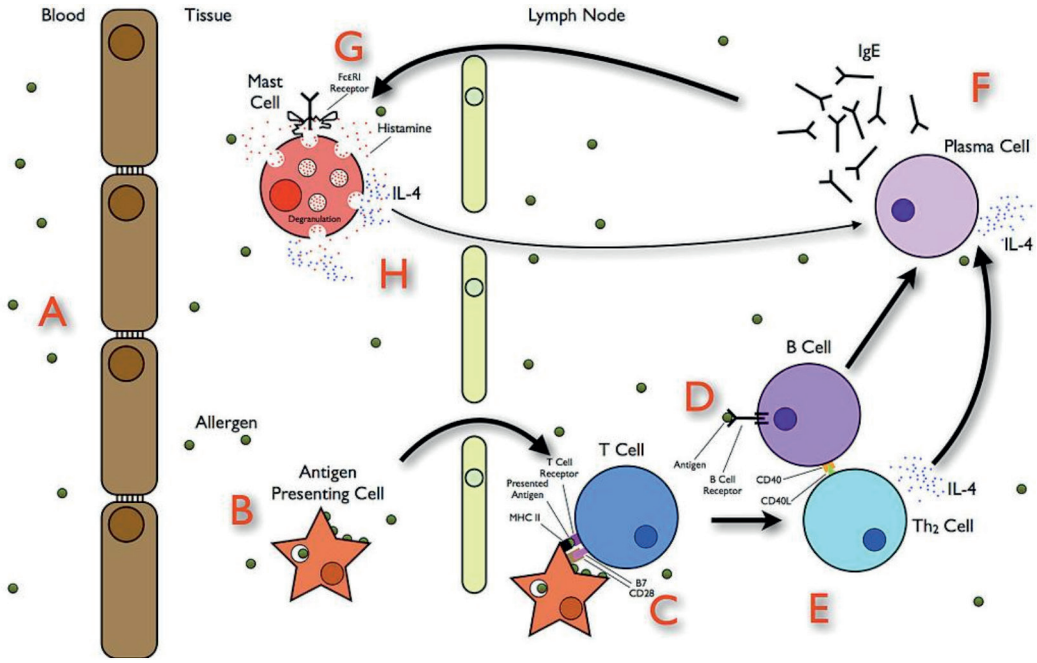

Figure 1. The basic cycle of allergic reaction.

of confirmed clinical treatment practices. So far only rescue medication is in use for emergent accidental reactions. There is no established treatment for its cure in routine clinical practice. However, discontinuation of the food involved in allergy is highly recommended. Further, most of the times during accidental encounters rescue medicines are also prescribed[6]. Food allergy has the highest impact on the young children and is on continuous rise[7]. Allergens like egg, tree nuts and cow milk are the most commonly reported allergens. Further, anaphylaxis is the most frequent form of food allergy observed especially in children[7-9]. Despite advances in bio-medial sciences, the reason for the huge spread of food allergy is cow milk. The cow milk is very difficult to avoid due to availability in multiple food forms[10]. Other causes include in-appropriate use of medicines, phobia intrusions towards injections, etc.[11].

Latest Management Avenues for Food Allergy

Various strategies are being investigated for the efficient management of food allergy. The oral immune therapy (OIT) is the latest and the most frequently reported strategy against food allergy. OIT involves increase in the intake of food responsible for allergy in the patient on regular basis. This process in turn, modulates internal immune response by making immune system unresponsive towards food allergen concerned[12]. Moreover, OIT helps in desensitization of the affected by enhancing its threshold dose of allergen by repeated exposures. Despite frequent reports, it is not the gold standard therapy due to associated risk of fatal allergenic reactions[13-15]. Also, the reports supporting its clinical use are not enough in patient number to make the positive facts certain for this form of therapy. Further, researchers are working on the improvisations of OIT by exploiting modified hypo allergens for immunomodulation. The use of specific biomarkers for safety aspects of OIT is also evolving. Other latest strategies for food allergy management, included Epicutaneous immunotherapy. This includes exposure of a specific food allergen instilled in a patch and the same is put on the skin of the affected patient for immune-modulation. The presence of high numbers of antigen presenting cells in epidermal layer helps in better efficacy. On the other hand, poor vascularization helps in prevention of unwanted systematic allergic reactions[16]. Furthermore, use of sublingual route is another strategy for the management of food allergy, known as sublingual immunotherapy (SLIT)[17].

Use of Hypo Allergens

Another important way to tackle food allergy from a specific allergen like milk is the use of its hypo-allergic form for immunomodulation pur-

pose. In recent past, heated cow milk have been found to be tolerable in the 70% of allergic children[18]. The working mechanism was found to be the protein structure modification of the milk that prevented binding of IgE antibody[19]. Another recent approach is to form engineered recombinant proteins in the food allergens to decrease allergic reactions[20].

Asthma and its Management

Asthma is the prevalent chronic disease affecting more than 300 million people worldwide[21]. Asthma is often classified as "allergic" or "non-allergic". Further, most of the cases of allergic asthma are IgE-mediated[22]. At present, no specific treatment for the allergic asthma is available. However, symptomatic control is realized by inhalation of steroids, use of beta-2 agonists, antileukotrienes, theophylline, anti-IgE antibodies and anticholinergic drugs[23].

Latest Management avenues for Allergic Asthma

Frequent wheezing in young children often is found to be a prominent symptom of asthma at later stage in affected young patient[24]. Moreover, it has now become one of the prominent symptom to certain the risk of asthma allergy especially in children with IgE sensitizations[25,26]. Observation of frequent wheezing (recurrent) without any upper airway blockage or infection is the clear indication of the risk of IgE sensitive asthma[27]. Further, in addition to IgE testing, lung function testing, bronchial hyper-responsiveness evaluation and bronchial inflammation testing are some of the confirmatory tests for allergic asthma in children[28].

The latest management avenue for asthma is the allergen immunotherapy (AIT). It holds promising treatment potential against respiratory allergy. The principle of action is similar to oral immunotherapy[29]. Moreover, epigenetics is another upcoming area, which is proving effective in various pathological states including asthma. Epigenetics in Asthma could effectively transduce environmental signals linked with asthma[30,31]. In support of epigenetics in asthma, recent studies identified epigenetic signatures like DNA methylation as the confirmation of asthma[32,33]. However, specific DNA methylation patterns linked with asthma are very modest. So, this caused great confusion for clinical application[34]. Moreover, epigenetic approach is in its preliminary stage and further studies are required to establish it as a clinical management avenue for asthma[35].

Rhinitis and its Latest Management Avenues

Rhinitis is classified as allergic or non-allergic rhinitis, and most cases of the allergic rhinitis are IgE mediated. Allergic rhinitis could be seasonal (often pollen-induced) or perennial. Further, approximately 8.3% of children are affected and are aged between 6-7 years. Further, it is more prominent in children with age between 12-14 years[36]. Common symptoms are snuffling, sneezing, nasal pruritus and congestion[37].

Pharmacotherapy is the method of choice for seasonal rhinitis and has been reported be quite effective. However, resistance to common pharmacotherapy is the first sign of perennial allergy. The most acceptable treatment avenue is the use of intranasal corticosteroids (INS) especially in children[38,39]. INS therapy is well established and has proved its efficacy in both adults as well as adolescents. However, the results of systematic review in a recent past have shown that INS therapy is weak and unreliable in children[40]. Further, MP-AzeFlu is another recent effective approach against allergic rhinitis. It is basically an intranasal antihistamine reported to be efficient as well as safe for both adults as well as adolescents[41,42]. Moreover, Food and Drug Agency (FDA) have recently approved it for pediatric use.

Atopic Dermatitis/Eczema

The atomic dermatitis/Eczema is the allergy-associated disease of skin found commonly in children. The widely reported pathogenesis of the allergic reaction have confirmed the observation of dry skin mediated by genetic mutations[43]. The route of exposure to the allergen for this reaction is food[44]. So, the management avenues for this pathological state are also similar to that of food allergy as it is somehow food-associated allergy only.

Allergic Sensitization and its Diagnostic Tests

The presence of specific immunoglobulin E (sIgE) against common environmental antigens is referred as allergic sensitization. It usually develops during childhood as a result of interplay between genetics and environment[45,46]. Furthermore, diagnosing inhalant and resultant allergy could be challenging as they vary in severity. Furthermore, the same child could express symptoms with different degree of severity when exposed to the same allergen at different time-points[45]. The mild cases of both inhalant and allergy are often misinterpreted because symptoms could be

diffused or non-specific[47]. So, basic tests in use for allergy sensitization, included skin prick testing (SPT) and measurement of serum specific IgE (sIgE) levels. Advantages of SPT are that it is economic, easy to perform and has no discomfort[48]. Disadvantages included skin rash and pain especially, in sensitive children. However, rash-free skin creams with antihistamine properties are available for testing. On the other hand, advantages of sIgE test, is no special requirement for rash-free skin. Moreover, the test results are delayed, costs are higher and there is noteworthy discomfort for the child when obtaining the blood sample in sIgE testing[48]. SPT results and serum levels of sIgE are often used interchangeably for diagnosing allergic sensitization in clinical practice and research[49,50]. However, many studies have confirmed that correlation seems to rely on the age of the child and allergen in question[51].

CRD in Allergic Sensitization Diagnosis

The component resolved diagnosis (CRD) of sensitization marks a new era in the field of allergy and immunology. This novel way of characterizing sensitization could help to identify sensitization to specific proteins and molecular components of the allergens[52]. The most recent protein microarray ImmunoCAP (ISAC) Immuno Solid-phase Allergen Chip® offers the possibility of analyzing specific IgE (sIgE) against 112 components from 51 different allergenic sources using just 50 μL of serum. The CRD provides an opportunity to identify different phenotypes of sensitization. It is basically based on biologically meaningful categorizations according to protein-groups, without the need of complex statistical models.

Conclusions

It is quite evident from the above literature that researchers are involved in the searching novel way of analyzing and interpreting allergen sensitization. Different clinical phenotypes based on protein-group sensitization offer new perspectives for both researchers and clinicians. Furthermore, future studies are required for establishment of more accurate, specific and efficient avenues for management of allergy disorders.

Conflict of Interest

The Authors declare that they have no conflict of interest.

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