FOOD ALLERGY AND ASTHMA EXACERBATION IN ASTHMATIC CHILDREN

Thesis
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سبحانك اللطيف القيم
إلا ما وعمنا إنك أنت
العلم الأعظم

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**Introduction**

The prevalence of asthma and allergic diseases among children and adolescents has rapidly increased over the last 10 years, especially in the western world, and it has become a serious public health issue. Unfortunately, the reasons for this increase are still obscure but risk factors including genetic predisposition and environmental factors (change in lifestyle, air pollution, etc.) could be responsible. In fact, one hypothesis to explain the occurrence of asthma and allergies in childhood, are related to lifestyle factors. Among these factors, dietary habits may be one of the contributing factors *(Saadeh, et al.,2013).*

Several studies have shown that some food could increase the risk of asthma and allergies, while others hypothesize that other food products could have a protective effect on allergies, such as vegetables, and oily fish. Dietary fat intake was shown to have an association with atopy in children. Therefore, high margarine consumption was positively associated with hay fever, while butter consumption was negatively associated with hay fever. Furthermore, protein-rich and fat-rich foods of animal origin were associated with a higher prevalence of asthma *(Armentia et al.,2001).*

Special attention was given to n-3-poly unsaturated fatty acids (PUFA) intake. In fact, there is evidence that fish rich in n-3-PUFA has antiinflammatory properties and may modulate the immune response towards a Th1 type. In fact, fish consumption was shown to have a protective effect on childhood asthma in several studies.
Moreover, in the ISAAC, ecological studies suggested a relationship between the intake of trans-fatty acids and the prevalence of childhood asthma and allergies, and a consistent inverse relationship was seen between prevalence rates of asthma, allergic rhinitis and eczema and the intake of vegetables. Furthermore, decreased intake of antioxidants found mostly in fresh fruit and vegetables, has been shown to have a role in the development of atopy (Devereux et al., 2005).

Determining the prevalence of food hypersensitivity and food allergy is a complex issue due to the different cultures, dietary habits, and geographical and regional differences of allergen distribution. It is still unclear if the prevalence of food allergy is continuously rising although many studies conclude that there is a rising trend at least in western and developing countries (Chafen et al., 2010).

The relationship between asthma and food allergy has also been discussed but the available data demonstrating a common pathogenetic mechanism are still few. In adults this relation was often denoted by case-reports, which claim that food hypersensitivity may trigger or affect asthma symptoms. It has been shown previously that having asthma might be a risk factor for a fatal food reaction and having food allergy might be a risk for complicated or poorly controlled asthma (Berns et al., 2007). Oehling et al. has previously shown that one third of children with food allergy also have asthma and about 4-8 % of children with asthma have food allergies (Oehling et al., 1980).
The prevalence though of food allergy in adults with asthma is still not known. However, it has been demonstrated that adult patients with one or more food allergies had increased hospitalizations for asthma, and in a study from Woods et al., it was shown that adults with probable peanut and shrimp allergy often have more frequent asthma episodes and doctor’s diagnosed asthma. In addition, it has been also shown that inhalation of aerosolized food particles may lead to the development of asthma in adults (Woods et al., 2002).

A study on children by found a possible correlation between asthma and gastrointestinal symptoms. In a previous study from a relation between food allergy and concomitant asymptomatic bronchial hyper-reactivity could be shown. The notion that there is a probable relation between asthma and gastrointestinal symptoms in adults was supported previously in a study which confirmed that asthmatics generally experienced more gastrointestinal symptoms than the non-asthmatic population (Powell et al., 2007).
**Aim of the work:**

We aimed to assess:

- Association of asthma and food allergy.
- Asthma exacerbation and dietary factors.
- Asthma control and diet in asthmatic children.
Bronchial Asthma

Definition:

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation. (GINA, 2021).

Epidemiology:

Asthma affects an estimated 300 million individuals worldwide. Evidence shows that the prevalence of asthma is increasing, especially in children. Annually, the World Health Organization (WHO) has estimated that 15 million disability-adjusted life-years are lost and 250,000 asthma deaths are reported worldwide (GINA, 2010).

Few studies evaluated asthma prevalence as 4.8% in Egypt (Khallaf et al., 1993) and 8.2% in Egypt (EL-Hefny et al., 1994). In Cairo, prevalence of wheezing was 14.7% and the physician diagnosed asthma was 9.4% (Georgy et al., 2006). The prevalence of asthma among school children in Nile Delta region was 7.7% (Zedan et al., 2009).
**Classification of asthma:**

*a) Classification according to severity:*-

**Table I:** Classification according to severity

<table>
<thead>
<tr>
<th></th>
<th>Daytime symptoms</th>
<th>Nighttime awaking</th>
<th>FEV1, PEF variability</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mild Intermittent</strong></td>
<td>≤2 times/week</td>
<td>≤2 times/month</td>
<td>&gt; 80% of predicted &gt; 20%</td>
</tr>
<tr>
<td><strong>Mild persistent</strong></td>
<td>&gt;2 times/week</td>
<td>3-4 times/month</td>
<td>≥ 80% of predicted 20 – 30 %</td>
</tr>
<tr>
<td><strong>Moderate persistent</strong></td>
<td>Daily Attacks affect activity</td>
<td>&gt; 1 time/week</td>
<td>60% - 80% of predicted &gt; 30 %</td>
</tr>
<tr>
<td><strong>Severe persistent</strong></td>
<td>Throughout the day with Continuous limitation of physical activity</td>
<td>Frequent</td>
<td>&lt; 60% of predicted &gt; 30%</td>
</tr>
</tbody>
</table>

*(Liu Andrew et al., 2007)*

*b) Asthma phenotypes*

Asthma is a heterogeneous disease, with different underlying disease processes. Recognizable clusters of demographic, clinical and/or pathophysiological characteristics are often called ‘asthma phenotypes’. In patients with more severe asthma, some phenotype-guided treatments are available. However, no strong relationship has been found between specific pathological features and particular clinical patterns or treatment responses. More research is needed to understand the clinical utility of phenotypic classification in asthma.
Many clinical phenotypes of asthma have been identified. Some of the most common are:

- **Allergic asthma:** this is the most easily recognized asthma phenotype, which often commences in childhood and is associated with a past and/or family history of allergic disease such as eczema, allergic rhinitis, or food or drug allergy. Examination of the induced sputum of these patients before treatment often reveals eosinophilic airway inflammation. Patients with this asthma phenotype usually respond well to inhaled corticosteroid (ICS) treatment.

- **Non-allergic asthma:** some patients have asthma that is not associated with allergy. The cellular profile of the sputum of these patients may be neutrophilic, eosinophilic or contain only a few inflammatory cells (paucigranulocytic). Patients with non-allergic asthma often demonstrate less short-term response to ICS.

- **Adult-onset (late-onset) asthma:** some adults, particularly women, present with asthma for the first time in adult life. These patients tend to be non-allergic, and often require higher doses of ICS or are relatively refractory to corticosteroid treatment. Occupational asthma (i.e. asthma due to exposures at work) should be ruled out in patients presenting with adult-onset asthma.

- **Asthma with persistent airflow limitation:** some patients with long-standing asthma develop airflow limitation that is persistent or incompletely reversible. This is thought to be due to airway wall remodeling.
• **Asthma with obesity:** some obese patients with asthma have prominent respiratory symptoms and little eosinophilic airway inflammation.

There are limited data about the natural history of asthma after diagnosis, but one longitudinal study showed that approximately 16% of adults with recently diagnosed asthma may experience clinical remission (no symptoms or asthma medication for at least 1 year) within 5 years.11

Additional information can be found in Appendix Chapter 2 about factors predisposing to the development of asthma, and in Appendix Chapter 3 about pathophysiological and cellular mechanisms of asthma.

c) **Classification according to etiology:**

Asthmatic children can be presented with one or more of the following presentations:

1) **Extrinsic atopic asthma:**

The term extrinsic asthma has been used to describe patients whose asthma is triggered by exposure to inhaled aero-allergens. Atopy is defined by presence of abnormal amount of IgE antibodies in response to contact with environmental antigens and can be manifested as asthma, eczema, or seasonal and perennial allergic rhinitis. This can be demonstrated by the presence of elevated total or specific serum IgE levels in the blood or by demonstrating positive skin prick test to a variety of standardized aero-allergens *Braman, 2003*.

2) **Intrinsic asthma:**

Non allergic asthma (intrinsic asthma) refers to a population of asthmatics in whom there is no evidence of IgE mediated
hypersensitivity, I,E; skin tests to a wide variety of common inhalant allergens are negative. This form of asthma accounts for 40% of adult asthmatics, 10% of childhood asthmatics and demonstrates histological and biochemical features that are strikingly similar to asthma that is associated with allergy. Thus, Prior studies have suggested that they represent the same immune-pathologic entity, although the initiating mechanism are necessarily different (Allen et al., 2005).

3) Drug induced asthma:

In some asthmatic individuals, aspirin and other non steroidal anti-inflammatory drugs (NSAIDs) exacerbate the condition. This distinct clinical syndrome called aspirin-induced asthma (AIA) (Harold et al., 2003).

The prevalence of the syndrome in the adult asthmatic populations is approximately 4-10%. The etiology of AIA is complex and not fully understood, but most evidence points towards an abnormality of arachidonic acid (AA) metabolism. Cyclo-oxygenase (COX) , the rate limiting enzyme in AA metabolism, exists as two main iso-forms. COX-1 is the constitutive enzyme responsible for synthesis of protective prostanoids, whereas COX-2 is induced under inflammatory conditions. A number of theories regarding its pathogenesis have been proposed. The shunting hypothesis proposes that inhibition of COX-1 shunts AA metabolism in airway from production of protective prostanoids towards cystienyl leukotriene (Cys-LT) biosynthesis, resulting in broncho-constriction and increased mucous production. The COX-2 hypothesis proposes that aspirin causes a structural change in COX-2 that results in the generation of products of the lipo-oxygenase pathway. It is speculated
that this may result in the formation of mediators that cause respiratory reaction in AIA (Ahmed et al., 2004).

4) **Exercise-induced asthma:**

Terms exercise-induced asthma (EIA) or exercise induced broncho-constriction (EIB) are used to describe transient broncho-constriction occurs during or immediately after vigorous exercise in some subjects (Hildebrand, 2011).

Exercise induced broncho-constriction (EIB) is a consequence of evaporative water loss in conditioning the inspired air. The water loss causes cooling and dehydration of the airway surface. One acute effect of dehydration is the release of mediators, such as prostaglandin, leukotriens, and histamine, that can stimulate smooth muscle ,causing contraction and change of the vascular permeability. Inspiring cold air increases dehydration of the surface area and causes changes in bronchial blood flow. This proposes that the pathogenesis of EIB is related to the epithelial injury arising from breathing poorly conditioned air at high flows for long periods of time or high volumes of irritant particles or gases. The evidence to support this proposal comes from many markers of injury. The restorative process after injury involves plasma exudation and movement of cells into the airways. This process has the potential to expose smooth muscle to a wide variety of plasma and cell-derived substances. The exposure to these substances over time can lead to an alteration in the contractile properties of smooth muscle , making it more sensitive to mediators of broncho-constriction (Sandra, 2008).

5) **Cough-variant asthma:**
Cough variant asthma (CVA) is a form of asthma, which presents solely with cough. CVA is one of the most common causes of chronic cough. More importantly, 30-40% of adult patients with CVA, unless adequately treated, may progress to classic asthma. CVA shares a number of patho-physiological features with classic asthma such as atopy, airway hyper-responsiveness, eosinophilic airway inflammation and various features of airway remodeling. Inhaled corticosteroids remain the most important form of treatment of CVA as they improve cough and reduce the risk of progression to classic asthma most likely through their prevention of airway remodeling and chronic airflow obstruction (Niimi, 2011).

6) Nocturnal asthma:

Nocturnal symptoms and overnight changes in lung functions are a common part of the asthma clinical syndrome. An extensive body of research has demonstrated that nocturnal symptoms of cough and dyspnea are accompanied by circadian variations in airway inflammation and physiological variables including airflow limitation and airways hyper-responsiveness. Alterations in beta2-adrenergic and glucocorticoid receptors and hypothalamic-pituitary-adrenal axis function might play a role in modulating the nocturnal asthma phenotype, and recent studies have suggested that neuro-hormonal controllers of circadian rhythms, might be important as well (Sutherland, 2005).