Study of IL 13 in blood and induced sputum in patients with allergic asthma before and after rush and classic specific antigen immunotherapy

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دراسة انترلوكين رقم ثلاثة عشر في الدم والـ بـ صاق الـمـ سـ تحث في مرضي الربو الشعبي قبل وبعد اللقاح المناعى بالطريقة السريعة والطريقة العادية

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Introduction

Asthma is an inflammatory disorder of the lungs that affects people of all ages and is a significant source of morbidity and mortality worldwide. Approximately 300 million people in the world currently have asthma and recent decades have shown a considerable increase in the prevalence of this condition in both children and adults **[1]**.

There has been considerable increase in the prevalence of asthma in both children and adults, If the current trends continue, it is estimated that there may be an additional 100 million more asthmatics by 2025 **[2]**.

Specific antigen immunotherapy (SIT) has been used successfully for the management of allergic disorders, including allergic asthma, and seasonal and perennial allergic rhinitis **[3]**.

Classic SIT using a protocol of gradually increasing dosages of allergen extract until a maintenance dose is reached, has been used for the management of allergic disorders, including allergic asthma, and seasonal and perennial allergic rhinitis. Despite the clear benefits of classic SIT, its major inconvenience is the extended treatment duration required, including a build-up phase which may range up to a few months, depending on the frequency of the injections. For this reason, rush immunotherapy (RIT) has been suggested as an alternative to classic SIT. RIT involves a very short build-up phase of only a few days to reach the effective maintenance dose, and provides better compliance because of its more immediate efficacy, allowing patients to appreciate the benefits of immunotherapy much sooner **[4]**. The major controversy surrounding RIT is its potentially increased risk of systemic reactions

[5]. As with conventional SIT, RIT decreases airway inflammation and airway hyper-responsiveness, and shifts cytokine production from the Th2 type to the Th1 type **[6]**.

Aim of the work

The aim of this study is to detect the role of IL 13 in the pathogenesis of allergic asthma and to measure the changes after using rush and classic specific antigen immunotherapy.

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List of abbreviations

ASM	Airway smooth muscle
BAL	Bronchoalveolar lavage
DC	Dendritic cell
EPR3	Expert Panel Report 3
FeNO	Fractionated exhaled nitric oxide
FEV1	Forced expiratory volume in 1 second
FVC	Forced vital capacity
HDM	House dust mites
ICS	Inhaled corticosteroid
IL	Interleukin
IL-4Rα	IL-4 receptor α
L-13Rα1	IL-13 receptor α 1
IFN	Interferon
LABA	Long-acting β-agonist
MHC	Major Histo-compatibility Complex

NAEPP	National Asthma Education and Prevention Program
NHBE	Normal human bronchial epithelial cells
NKT	Natural killer T
RAST	Radioallergosorbent test
RIT	Rush immunotherapy
SABAs	Short-acting beta-2 agonists
SCIT	Subcutaneous immunotherapy
SIT	Specific antigen immunotherapy
SLIT	Sublingual immunotherapy
TCR	T cell receptor
Tfh	T follicular helper
TGF-β	Transforming growth factor-beta 2
TNF	Tumor Necrosis Factor
Tregs	Regulatory T cells

Asthma

Definition of Asthma:

World Health Organization defined Asthma as a disease characterized by recurrent attacks of breathlessness and wheezing, which vary in severity and frequency from person to person. In an individual, they may occur from hour to hour and day to day, this condition is due to inflammation of the air passages in the lungs and affects the sensitivity of the nerve endings in the airways so they become easily irritated. In an attack, the lining of the passages swell causing the airways to narrow and reducing the flow of air in and out of the lungs **[7]**.

Epidemiology of Asthma:

The recent substantial increase in the reported prevalence of asthma worldwide has led to numerous studies of the prevalence and characteristics of this condition **[8]**. Foremost among these are 2 major international initiatives that have collected data using validated questionnaires, one among children, the International Study of Asthma and

Allergies in Childhood **[9]**, and the other among young adults, the European Community Respiratory Health Survey **[10]**. Follow-up investigations for both of these have examined temporal trends within and across populations. During a mean of 7 years following phase I of the International Study of Asthma and Allergies in Childhood, which in most participating countries was conducted between 1991 and 1993, the prevalence of asthma was stable or decreased in some areas of the world but increased substantially in many other areas especially among children 13–14 years of age **[11]**.

The prevalence of asthma symptoms in Cairo, Egypt:

In a study by Fahim et al (2006) on the Prevalence and socioeconomic associations of asthma and allergic rhinitis in Cairo, Egypt, the study found that the prevalence of physician diagnosed asthma in school children in Cairo was 9.4%; there is a higher prevalence and increased severity of asthma symptoms in children of lower socioeconomic group as defined by state school attendance in Cairo **[12]**.

Etiology and risk factors for asthma:

Genetic factor:

Many genes have been documented to affect the familial occurrence of asthma, familial features of the components of response to a variety of indoor and outdoor allergens, and the mode of inheritance of asthma. In several large population-based studies, asthma and asthma-associated phenotypes were shown to exhibit significant familial correlations with multiple major genes **[13].**

A numerous genome-wide screens have been published, and from these studies, 6 genes have been identified to be linked with asthma **[14]**.

The National Heart, Lung, and Blood Institute funded a multicenter Collaborative Study on the Genetics of Asthma **[15]**.

The Collaborative Study on the Genetics of Asthma studied families from different ethnic groups and different geographic sites. More than 15 linkage regions were identified that contributed strongly to asthma

susceptibility, including several sites in previously unsuspected areas of the human genome **[16]**.

Pharmacogenetic factors:

Pharmacogenetics is defined as the study of variation in drug response due to differences in the genetic composition of individuals. Genetic variations in drug target genes can predict clinical responsiveness to treatment.

The gene encoding the beta2-adrenergic receptor (ADRB2) is one of the most extensively studied genes; it is a small gene that encodes a 413-amino acid protein. , the amino acid changes may affect receptor regulation in various ways including alterations of agonist binding affinity, downstream signal transduction, or receptor trafficking **[17]**.

pharmacogenetic factors also proved to affect the response to inhaled corticosteroids as well as to Leukotriene receptor antagonists **[18]** and **[19]** .

Outdoor environmental factors:

Several outdoor pollutants have been associated with increases in visits to emergency departments for asthma **[20]**.

In a controlled study it was shown that subjects with asthma are sensitive to inhaled Sulfur dioxide. Inhalation of Sulfur dioxide for 10 minutes during moderate exercise can decrease FEV1 by 23% and increase total lung resistance by an average of 67% **[21]**.

Smoking and Environmental tobacco smoke:

Several studies had demonstrated an accelerated decrease in lung function over time in asthmatic individuals who smoke **[22]**.Adults and older children with asthma who are active smokers have more severe symptoms and worse asthma-specific quality of life compared with asthmatic nonsmokers, with asthma morbidity and mortality being reported to be greater in cigarette smokers with asthma compared with that in those who never smoked **[23]**.

Moreover a reduced therapeutic response to inhaled and oral corticosteroids in asthmatic patients who are cigarette smokers has been reported **[24]**.

Reliable evidence proved that exposure to environmental tobacco smoke is linked with impaired lung function and aggravation of asthma in childhood, asthmatic children with mothers who smoke were found to have more severe asthma when compared with those whose mothers did not smoke **[25].**

Gene environmental interaction in childhood asthma:

The interaction between numerous environmental influences and the genetic predisposition makes asthma a complex disease in which the effects of single genetic or environmental factor may be hard to detect and to evaluate, so mixed models of genetic and environmental influences gave the best match with the observed distribution of asthma **[26**].