Study The Role of Natural Killer T Cells in Asthmatic Children.

Thesis
Submitted for Partial Fulfillment
of
Master Degree in Pediatrics
By

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دراسة دور الخلايا تى الليمفاوية القاتلة الطبيعية في مرضى الربو الشعبي من الأطفال

رسالة

مقدمة من الطبيب /شوقي عبد العزيز ذكى
بكالوريوس الطب والجراحة 2000
طب عين شمس

توطئة للحصول على درجة الماجستير في طب الأطفال

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القاهرة 2009

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INTRODUCTION

Pediatric bronchial asthma is considered a common chronic illness in childhood **(Sidwell and Thomson, 2000).**

Studies suggested that therapies targeted at depletion or limiting of natural killer T cells may be a possible strategy for the treatment of asthma **(Bendelac et al., 2003).**

Many natural killer T cells express a highly restricted repertoire of T cells receptors consisting of V alpha 24 in humans and are called invariant T cell receptor- positive natural killer T cells (invariant NKT cells) (**Taniguchi et al., 2003).**

On activation of invariant natural killer T cells, They rapidly produce large quantities of both type I helper (Th_1)-biased (interferon–gamma) and Th2-biased cytokines (interleukin-4), Which enhance the function of dendritic cells, and B cells, as well as the function of conventional CD4+ and CD8+ T cells (**Kronenbreg M and Gapin L, 2002).**

As the role of invariant natural killer T cells in asthma is not well evaluated, We study the frequency distribution of restricted invariant natural killer T cells (TCR V α 24 NKT cells) in peripheral blood of known cases of asthmatic children **(Akbari et al., 2006).**

The aim of study was:

To assess the role of TCR V alpha 24 invariant natural killer T cells in asthmatic children and detection of TCR V alpha 24 invariant NKT cells in peripheral blood in asthmatic children .

PEADIATRIC BRONCHIAL ASTHMA

Definition:

Asthma is a major health problem. It is the most common chronic childhood diseases (**Liu et al., 2004**).Acute exacerbation of asthma are the leading cause of emergency department visits in the pediatric patients (**Fernandez, 2005**). In addition asthma is responsible for a significant problem of school day loss (**Liu et al., 2004**).

Asthma is defined as reversible obstruction of the airway, characterized by hyperresponsiveness to a variety of stimuli, caused by chronic inflammation. The airway obstruction is reversible, at least in part, and results in recurrent episodes of wheezing, cough, and shortness of breath that resolve either spontaneously or with treatment (**Keresmar, 2003).**

Asthma may have its onset at any age, 30% of patients are symptomatic by age of one year, which 80-90% of asthmatic children have their first symptoms before 4-5 years of age **(Sly, 2000).**

Although most cases begin before the age of 25 years asthma may develop at any time of life **(Drazen, 2000).**

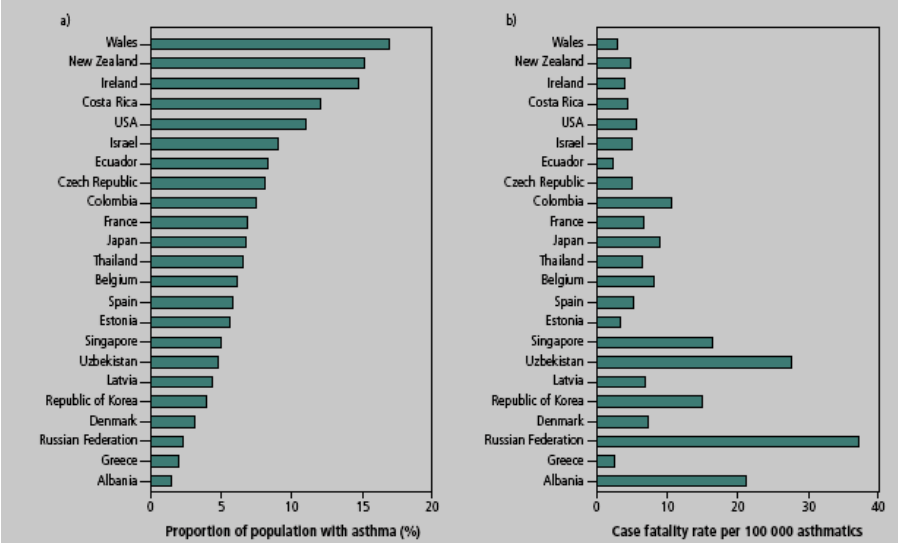
Epidemiology of pediatric asthma in Egypt:

In Egypt 23.2% of wheezy infants were proved to be real asthmatic **(El Hefney et al., 1991).**

The incidence of asthma among school children aged 5-15 years old was found to be 8.2% **(El Hefney et al., 1994).**

Abdel Latif (2000) studied the prevalence of asthma among 2321 secondary school (13-20 years old) in Four randomly selected districts (Misr El-Gedida, Helwan, Shoubra, Abbassia) and he reported a prevalence of pediatric asthma of 5.6%.

Figure (1): Prevalence and mortality from asthma :



(Bousquet et al., 2005)

Worldwide prevalence of asthma:

A asthma is one of the most common chronic diseases worldwide and the prevalence is increasing. Especially among children. The prevalence of asthma symptoms in children varies from 2 to 30 percent in different populations with the highest prevalence occurring in Australia, New Zealand and England **(GINA, 2005).**

Over the past 30 years, the prevalence of asthma has increased to epidemic proportion in developed countries, and asthma is the most common chronic disease in children **(Arroda et al., 2006).**

Risk Factors for Asthma:

(1) Genetic Factors:

The understanding of the genetic controls that lead to the development of asthma is essential to its proper diagnosis and management **(Blumenthal, 2002).**

Results from twin studies have consistently found evidence that genetic factors contribute importantly to asthma **(Koeppen- Schomerus et al., 2002).**

Asthma is a complex genetic disorder with variable phenotypes, largely attributed to the interactions of the environment and multiple genes **(Arroda et al., 2006).**

Asthma is essentially a polygenic disease in which many genetic variant determine small changes in immune responses

or in the manner in which the airway responds to the environment **(Holberg et al., 1996).**

The severity of asthma and response to treatment have also been suggested to be dependant on genetic modulators, such as the polymorphism of the ***B2***-receptor (found on chromosome 5), which is involved in the bronchodilator response to ***B-***agonists **(Ligget, 2000).**

(2) Gender and Asthma:

Gender differences in asthma prevalence and severity vary by age and may be attributed to differences in biologic susceptibility due to changes in hormonal milieu with aging, environmental exposures health care accessibility **(Caracta, 2003)**.

Males have more severe airway hyperresponsiveness ;this may be one factor contributing to the higher prevalence of asthma in boys **(Jenssen and Cockroft, 2003 and Abd El Khalek et al., 2003).**

Epidemiological studies of both incidence and prevalence, have reported a male predominance of asthma and atopic conditions before puberty and a female predominance after puberty. There is evidence that airway development is different between the sexes. In females, there is proportionate growth of airways to lung volume and as a consequence