Role of Human Rhinovirus Infection in the Expression of Asthma-Related SymptomS

Thesis

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By

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Abstract

Asthma is a leading cause of chronic illness in childhood. In the present case control study we evaluated the role of Human Rhinovirus infection in the expression of asthma-related symptoms.

The study was conducted on 40 children aged 6 to 14 years, were classified into two groups: (group A: first time wheezers =11 patients) and (group B: chronic known asthmatics presenting with acute exacerbation =29 patients). In addition to 20 healthy age matched control.

All subjects were subjected to a complete history and clinical study, and were investigated with emphasis on CBC with differential, CRP and total serum IgE. Chest X-ray was done to all subjects. Nasopharyngeal swabs were obtained from all subjects and the presence of Human Rhinovirus were determined by PCR examination.

The results as regards absolute eosinophilic count (AEC) and IgE were significantly higher in patients than controls (p value=<0.001) in both groups.

Positive PCR for Rhinovirus was detected in 1 (9%) in (group A= first time wheezers) and in 2 (6.8%) in {group B= known asthmatics during acute exacerbation).

In conclusion, the present study does not support that rhinovirus infection might promote first attack wheezing or acute exacerbation of known asthma.

Keywords: Asthma, Rhinovirus infection.

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In the name of Allah, the all mighty God, the one and only one, I hereby start my thesis.

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Norhan Noaman Mohamed El-Malkh

Contents

List of Abbreviations

AHR	Airway hyper-responsiveness.
APC	Antigen- presenting cells.
ATM	Adipose tissue macrophage.
BHR	Bronchial hyper-responsiveness**.**
BK	Bradykinen.
BMI	Body mass index.
CD14	Cluster of Differentiation 14.
COAST	The Childhood Origins Of Asthma.
CYSLTR	Cysteinyl leukotriene receptor.
DALYS	Disability adjusted life years.
EIB	Exercise induced bronchospasm.
ETS	Environmental tobacco smoke.
FDA	Food and Drug Administration.
FEF	Forced expiratory flow.
FEV	Forced expiratory volume.
FLG	Filaggrin.
FVC	Forced vital capacity.
GERD	Gastro-esophageal reflux disease.
GM-CSF	Granulocyte-macrophage colony- stimulating factor.
HDM	House dust mite.
HRV	Human rhinovirus.
ICAM-1	Intra-cellular adhesion molecule 1.
IFN	Interferon.
IgE	Immunoglobulin E.

IL	Interleukin.
LBK	Lysylbradykinin.
LTs	Leukotriens.
MDK	Macrophage derived chemokine.
NO	Nitric oxide.
NO2	Nitrogen dioxide.
O3	Ozone.
PCR	Polymerase chain reaction.
PEEF	Peak end expiratory flow.
PEFR	Peak expiratory flow rate.
PGD	Prostaglandins.
PM	Particulate matter.
QOL	Quality of life.
RAST	Radio allergosorbent test.
ROS	Reactive oxygen species.
RSV	Respiratory syncytial virus.
RT-PCR	Reverse transcriptase- polymerase chain reaction.
SLIT	Sublingual immunotherapy.
TCR	T cell receptor.
Th2	T-helper cell.
LR-3	**T**Toll like receptor-3.
TNF	Tumor necrosis factor.
TSLP	Thymic stromal lymphopoeitin.
VCAM-1	Vascular-cell adhesion molecule 1.
VEGF	Vascular endothelial growth factor.

WHO	The World Health Organization

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Introduction

Asthma is a heterogeneous and multifactorial disease manifested as episodes of wheezing, coughing, and shortness of breath particularly at night. Multiple genetic and environmental factors are also known to modulate the clinical expression of the disease and its associated phenotypes-bronchial hyper-responsiveness, atopy, and elevated IgE ***(Sleiman et al., 2010).***

The major pathophysiologic characteristics of asthma are bronchial inflammation and airway hyper-responsiveness, which result in episodes of reversible airway obstruction ***(Bousquet et al., 2007).***

Among the various factors that have been involved in asthma pathogenesis, viral infections are the most prominent. Viral infections affect wheezing and asthma in children and adults of all ages. Wheezing illnesses are usually viral in origin, and children with more severe wheezing episodes are more likely to develop asthma later on in childhood ***(Gavala et al., 2011).***

Human rhinoviruses are not only the main pathogens responsible for the common cold, but are now recognized to have a major impact on asthma pathogenesis. There is evidence that rhinovirus infections play a role in asthma development, asthma exacerbations and, potentially, airway remodeling. Children who experience repeated rhinovirus-induced wheezing episodes in infancy have a significantly increased risk of developing asthma, even when compared to children who experience wheezing induced by respiratory syncytial virus ***(Proud, 2011).***

The association between viral infections and asthma exacerbations has been illuminated by the development of sensitive diagnostic tests based on PCR and/or microarray technology, for viruses that are difficult to culture representing up to 85%-95% of asthma exacerbations in children with approximately two-thirds of these infections are caused by HRV ***(Guilbert and Denlinger, 2010).***

Aim of the Work

To evaluate the role of human rhinovirus infection in expression of asthma-related symptoms in patients presenting either with the first attack of wheezing began after an acute respiratory illness or chronic asthmatics previously following up at the pediatric Allergy & Asthma clinic.

Bronchial Asthma

Definition:

Bronchial asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role, in particular, mast cells, eosinophils, T-lymphocytes, macrophages, neutrophils, and epithelial cells. In susceptible individuals, this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment. Globally, people of all ages and all ethnic backgrounds suffer from asthma and the burden of this disease to governments, health care systems, families, and patients is increasing worldwide ***(Global Initiative for Asthma, 2008).***

Because there is no clear definition of asthma, phenotype researchers studying the development of this complex disease turn to characteristics that can be measured objectively, such as atopy (manifested by the presence of positive skin-prick test response to common environmental allergens), airway hyper-responsiveness (the tendency of airways to narrow excessively in response to triggers that have little or no effect in normal individuals) and other measures of allergic sensitizations ***(GINA, 2008).***