A STUDY OF INTERLEUKIN-4 AND INTERFERON-GAMMA AS PREDICTIVE INDICES FOR EARLY DETECTION OF ASTHMA IN WHEEZY INFANTS

Thesis
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بسم الله الرحمن الرحيم

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قالوا سبحانك لا علم لنا الا ما علمتنا

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Abstract

Childhood wheeze is common. It usually begins in early life, and may then persist into later life. Asthma is preceded by a stage of recurrent episodes of wheezing during the first years of life and proper treatment during symptomatic episodes may delay progression to persistent asthma. Th2 type cytokines,IL-4 is a as key regulator factor in asthma. INF-γ antagonizes IL-4-dependent IgE production. IL-4/ IFN-γ ratio was greater in children with asthma compared with control children The aim of this study is to determine the level of IL-4 and INF-gamma in early onset wheezy children to detect those who may develop asthma for early prevention and better prognosis.

Key words :

INTERLEUKIN-4 – INTERFERON – ASTHMA IN WHEEZY INFANTS

CONTENTS

LIST OF ABBREVIATIONS

AR	**Airway Responsivness**
PW	**Persistent Wheeze**
ICS	**Inhaled Cortocosteroids**
RSV	**Respiratory syncitial virus**
SR aw	**Specific Resistance of airways**
Th	**T helper**
IL	**Interleukin**
IgE	**Immunoglobulin E**
TGF	**Transforming Growth Factor**
IFN-γ	**Interferon Gamma**
WARI	**Wheezing Associated Respiratory infections**
RANTES	**Regulation on Activation Normal T Cell Expressed and Secreted**
ECP	**Eosinophil Cationic Protein**
PCR	**Polymerase Chain Reaction**
LPR	**Late Phase Reaction**
EGFR	**Epithelial Growth Factor Receptor**
ARS	**Adenosine Receptors**
FVC	**Forced Vital Capacity**
FEV1	**Forced Expiration Volume in One Second**
RTCS	**Randomised Control Trials**
PGS	**Prostaglandins**
APC	**Antigen Presenting Cells**
DCS	**Dendretic Cells**
GM-CSF	**Granulocyte Monocyte Colony Stimulating Factor**
PMNS	**Polymorph nuclear neutophils**
CFT	**Complement Fixation Test**

NK	**Natural Killer Cells**
PDGF	**Platelet-derived growth factor**
FGF	**Fibroblast growth factors**
VCAM-1	**Vascular cell adhesion molecule-1**
TNF-α	**Tumor necrosis factor alpha**
IL-1RA	**IL-1 Receptor antagonist**
ASM	**Airway smooth muscle**
NO	**Nitric oxide**
TGF-β	**Transforming growth factor β**
SCF	**Stem cell factor**
VIP	**Vasoactive intestinal polypeptide**
HIV	**Human immunodeficiency virus**
NAP-2	**Neutrophil activating protein 2**
GCP-2	**Granulocyte chemotactic protein 2**
Igf	**Insulin-Like Growth Factor**
VEGF	**Vascular endothelial growth factor**
CAPS	**Canadian Primary asthma Prevention Study**
FcεRI	**Fragment crystallizable Receptors with high- affinity for IgE**

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Introduction and Aim of the Work

CD4+T helper cells are strongly implicated in asthma pathogenesis. Immune responses to allergens are regulated by competing T helper 1 (Th1) and Th2 cell populations. Atopic disease is associated with Th2-skewed immune response to allergens **(Zdolsc et al 2003)**

Th2 type cytokines (interleukins IL-4, IL-5, IL-9, IL-13) regulate eoninophillia, mast cell growth, IgE, and mucus production and have been proposed as key regulator factor in asthma. Th1 type cytokines include interferon-gamma, IL-2, IL-12, IL-18, and tumor necrosis factor beta **(Anderson, 2002).**

Interferon-gamma (IFN-γ) antagonizes Interleukin-4 (IL-4) dependent IgE production as well as IL-5-induced proliferation an activation of eosinophils **(Biller et al, 2003)**

IL-4 and INF-γ are thought to play an important role in chronic airway inflammation in asthmatic subjects. In asthma there is increased expression of the Th2 type cytokine IL-4. IL-4 induces immunoglobulin E and adhesion of eosinophils to endothelium **(Fetich et al, 2003).**

The cytokine interleukin 12 (IL-12) is believed to play a central role in the regulation of immune differentiation of T lymphocytes. IL-12 is also produced by antigen-presenting cells (APCS) and its production is enhanced by microbial products such as lipopolysaccharides and viral nucleic acid **(Mallia and Johnston, 2002).**

The antiviral immune response is made up of innate (nonspecific) and specific components, and require the coordinated action of many different cell types including neutrophils, macrophages, eosinophils, dendritic cells,

epithelial cells, mast cells natural killer cells and B-and T-lymphocytes. Coordination of this response involves numerous cytokines and chemokins **(Message and Johnston 2001).**

It is believed that respiratory syncytial virus (RSV) may have unique effect on the infant respiratory tract in that it may be capable of inducing allergic sensitization and asthma. A positive association was reported between RSV of lower respiratory tract in infants and subsequent wheezing **(Sigurs et al, 2000).**

Infants experiencing severe respiratory syncitial virus (RSV) bronchiolitis have an increased frequency of wheeze and asthma in later childhood **(Culley et al, 2002).**

Th1 dysregulation associated with a Th2 response may modify the immune response to viral infection by altering the balance of T-cell cytokines from type 1 to type 2 in mixed immune response **(Message and Johnston 2001).**

Aim of the Work

As IL-4 is elevated and INF-γ is decreased in asthma. It is suspected to find similar changes in patients with prolonged or recurrent wheezy chest and these changes can be used as a prediction of early onset asthma. The aim of this study is to determine the level of IL-4 and INF-γ in early onset wheezy children with prolonged or recurrent wheezing whether following bronchiolitis or not to detect those who will develop asthma. As early diagnosis of early onset asthma has an important implication for early theraputic intervention and better prognosis.