A Study of The Relationship Between Airway Inflammation and Dipalmitoyl Phosphatidycholine in Induced Sputum of Asthmatic Children

Thesis
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Abbreviations

aa	Amino acid
AHR	Airway hyperresponsiveness
ARDS	Acute respiratory disease syndrome
BALF	Bronchoalveolar lavage fluid
bFGF	Basic Fibroblast growth factor
BMI	Body mass index
CAMP	Children Asthma Management Program
CCR	Chemokine receptor
CD40	Cluster of differentiation 40
CFC	Colony-forming cell
CO-2	Cyclooxygenase-2
COPD	Chronic obstructive pulmonary disease
DC	Dendritic cells
DPPC	Dipalmitoyl phosphatidylcholine
DSPs	Disaturated PLs
ECG	Electrocardiogram
ECP	Eosinophil cationic protein
EGF	Epidermal derived growth factor
EIA	Exercise-induced asthma
EOS	Eosinophils
EPO	Eosinophil peroxidase
EPX	Eosinophil protein X
$FEF_{25-75\%}$	Forced expiratory flow rate over 25-75% part of FVC
FEV_1	Forced expiratory volume in 1 second
FVC	Forced vital capacity
GER	Gastroesophageal reflux
GINA	Global Initiative for Asthma
GM-CSF	Granulocyte-macrophage colony-stimulating factor

HS	Hypertonic saline
IFN-γ	Interferon-gamma
IgE	Immunoglobulin E
IGF-1	Insulin-like growth factor
IL	Interleukin
ISAAC	International study of asthma and allergies in children
kDa	Kilodalton
LA	Large aggregates
LT	Leukotrien
MBP	Major basic protein
MC	Mast cells
MCP-1	Macrophage chemoattractant protein-4
MDC	Monocyte-derived chemokine
MMPs	Matrix metalloproteinases
NAEPP	National Asthma Education and Prevention Program
NANC	Non adrenergic non cholinergic
NCICAS	National Cooperative Inner-City Asthma Study
NGF	Nerve growth factor
NO	Nitric oxide
P	Pressure
$PaCO_2$	Arterial carbon dioxide tension
PAF	Platelet activating factor
PD-ECGF	Platelet-derived endothelial cell growth factor
PDGF	Platelet-derived growth factor
PEF	Peak expiratory flow
PFTs	Pulmonary function tests
PL	Phospholipid
r	Radius
RANTES	Regulated on activation of normal T cell expressed and secreted chemokines

RDS	Respiratory disease syndrome
RSV	Respiratory syncytial virus
SA	Small aggregates
SALP	Surface-active phospholipid
SaO_2	Anterial oxygen saturation
SCF	Stem cell factor
SD	Standard deviation
SP	Surfactant protein
T	Surface tension
TARC	Thymus- and activation-regulated chemokine
TCR	T-cell receptor
TGF-B	Transforming growth factor B
Th-0	Naive T-lymphocyte
Th2	T helper subset 2
TIMPs	Inhibitors of MMPs
TNF-α	Tumor necrosis factor-alpha
VCAM-1	Vascular cell adhesion molecule-1
VEGF	Vascular endothelial growth factor
VPF	Vascular permeability factor

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Introduction

Childhood asthma is a growing public health problem in the United States. The number of children affected by asthma grew 75% from 1980 to 1994. This increase was present for all children regardless of race, gender, or age. An increasing burden of asthma is placed on the youngest children: The prevalence of this condition increased 160% for children 0 to 4 years old from 1990 to 1994 ***(Steyer et al., 2003).***

Airway inflammation in asthma is extremely complex in origin, regulation, and outcome. The mechanisms involve a cascade of events involving many different kinds of cells, factors, and mediators that interact to create the characteristic inflammatory and tissue remodeling processes of asthma ***(GINA, 2003).***

In school children with atopic asthma, the limited data available indicate that the morphological picture with basement membrane thickening and inflammatory cell infiltration in the airway is similar to that encountered in adults, although not all studies have found eosinophilic inflammation. Basement membrane thickening has been demonstrated even in children with mild/moderate asthma ***(Barbato et al., 2003).***

Pulmonary surfactant is a unique mixture of lipids and surfactant-specific proteins that covers the entire alveolar, surface of the lungs. Surfactant is not restricted to the alveolar compartments; it also reaches terminal conducting airways and is present in upper airway secretions. While the role of surfactant in the alveolar compartment has been

intensively elucidated both in health and disease states, the possible role of surfactant in the airways requires further research ***(Hohlfeld, 2002).***

An intact and well functioning pulmonary surfactant system is critical for normal respiration and protection from lung infection. Alteration of surfactant composition and function occurs with various inflammatory disorders that affect the airways or the lung parenchyma including asthma ***(Meyer and Zimmerman, 2002).***

Aim of the work

The present work was carried out to investigate and assess the relationship between sputum and blood markers of inflammation [eosinophils, neutrophils, eosinophilic cationic protein (ECP)] to sputum diplamitoyl phosphatidy choline (DPPC) levels, as characteristic and major constituent of pulmonary surfactant in asthmatic children.

CHAPTER 1

PEDIATRIC BRONCHIAL ASTHMA

Definition:

Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation causes an associated increase in airway hyperresponsiveness that leads to 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 ***(GINA, 2003).***

Prevalence of asthma:

There are approximately 6.3 million children with asthma, admission rates for children young than 4 years of age with asthma are greater than those of other age group, and they account for a significant proportion of high annual rate in asthma mortality ***(Mannino et al., 2002).***

The prevalence of asthma symptoms in children varies from 0 to 30 percent in different populations. The international study of asthma and allergies in children (ISAAC) shows the prevalence of wheezing in the last 12 months –documented by written questionnaires – among children 13 to 14 years old in a number of populations.