Evaluation of Serum Lipoxin A4 in Exercise Induced Asthma

Thesis

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ABSTRACT

Background: Lipoxin A4 is a potent anti-inflammatory and several lipoxin forming multicellular interactions occur during strenuous

Aim of the study: to evaluate diagnostic value of lipoxin A4 as a biomarker of exercise induced asthma

Subjects and methods: This cross sectional study was conducted on forty-five asthmatic children divided in two groups; EIA group: 25 children with history of exercise-induced symptoms of asthma confirmed by spirometry, Non EIA group: 20 patients who did not have history of exercise induced symptoms of asthma. Forty-five apparently healthy children were included as a control group with no history of asthma or atopic conditions. Their age and sex were matched with the patients group. For all patients, pulmonary function tests were done before and after a free running test using portable spiromometery. Serum levels of lipoxin A4 were estimated for patients (after exercise) and controls using ELISA

Results: A significant difference was detected between the levels of lipoxin A4 in EIA and control groups (p value 0.000). There was significant difference between Non EIA and control groups regarding the level of lipoxin A4 with (P value 0.000). The mean level of lipoxin A4 in EIA patients was lower than that of Non EIA patients; however, the difference was statistically insignificant (P value 0.973).

Conclusion: Lipoxin A4 is a promising anti-inflammatory factor in management of asthma.

Keywords: Lipoxin A4, Exercise Induced Asthma, bronchial asthma

Contents

List of Abbreviations

15-Loa : 15-lipooxygenase a

15-Lob : 15-Lipooxygenase b

ABG : Arterial blood gass

APSGN : Acute poststreptococcal glomerulo-nephritis

ARF : Acute Renal Failure

ASL : Airway surface liquid

ASM : Airway smooth muscle

ATL : Aspirin-triggered lipoxins

B Blockers : Beta blockers

BAL : Bronchoalveolar lavage

BALF : Bronchoalveolar lavage fluids

BMI : Body Mass Index

CF : Cystic Fibrosis

CR3 : Chemokine receptor 3

COPD : Chronic Obstructive airway disease

EAR : Early phase Asthmatic Reaction

ECT : Exercise Challenge Test

EIA : Exercise Induced Asthma

EIB : Exercise induced Bronchoconstriction

EIIS :Exercise induced inspiratory stridor

ELISA : Enzyme-linked immunosorbent assay

EMTU : Epithelial Mesenchymal Trophic Unit

FEF25-75 : Forced expiratory flow at 25-75%

FEV1 : Forced Expiratory Volume in 1st Second

FVC : Forced Vital Capacity

GERD : Gastro-esophageal reflux disease

GINA : Global Initiative for Asthma

GWA :Genom world association

GPCR :G protein coupled receptor

HRP :Horseradish peroxidase

ICS :Inhaled corticosteroids

ICU : Intensivecare unit

IFN alpha: Interferon alpha (IFN α)

IFN gamma: Interferon gamma (IFN ¥)

IgE : Immunoglobulin E

IL : Inter leukin

LABAs **:**Long-acting beta$_2$-agonists

LTB4 : Leukotriene B4

LTD4 : Leukotriene D4

LT : Leukotriens

LX : Lipoxins

MPA : Major Basic Problem

MDC :Macrophage derived chemokines

MMEF :Maximum mid expiratory flow

MVV : Maximum Voluntary Ventilation

NK :Neutral killer

NSAIDs : Non Steriodal Antiinflammatory drugs

PAF **:** Plateles activating factor

PEF : Peak expiratory flow

PEFR : Peak expiratory flow rate

PFTs : Pulmonary Function Tests

PFho-lipoxinA4-Me: Para fluro-phenoxy LipoxinA4 methyl ester

PG : Prostaglandin

PGE **:** Prostaglandin E

PMN : Polymorph neucleocytes

SABA : Short acting B2 agonist

SST :Serum separator tube

TARC :Thymus activation regulated chemokines

Th : T- helper cell

TGFB : Transforming growth factor beta

TNF α : Tumor necrosis factor alpha

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Introduction

Bronchial asthma is a chronic disease of respiratory tract constituting a serious public health problem all over the world. Asthma prevalence has increased very considerably in recent decades such that it is now one of the commonest chronic disorders in the world **(Anandan et al., 2010).**

Asthma is characterized by a chronic inflammation of the airways. It leads to a variable airflow obstruction and symptoms such as wheezing, chest tightness, coughing, and dyspnea. Chronic inflammation observed in asthma leads to airway hyper-responsiveness that is defined as abnormal increase in airway flow limitations following exposure to non-allergic stimulus as exercise **(Tahan et al., 2008).**

Asthma affects about 300 million people worldwide. It is the most common chronic disease among children **(GINA, 2009)**, affecting nearly 5 million, children younger than age 18 in US. In Egypt 23.2% of wheezy infants were proven real asthmatics. Asthma prevalence among school children aged 5-15 years was found to be 8.2%, half of which are graded as moderate or severe **(Deraz, 2003).**

Exercise induced asthma (EIA) can be demonstrated in up to 70% of patients with asthma, and in other individuals who have (EIA) in the absence of additional features of asthma**.** The pathogenesis of (EIA) is poorly understood. Although conditioning of the inspired air, leading to drying and cooling of the intra-thoracic airways, may serve as the initial trigger for (EIA), the subsequent events in the airways are unclear **(Belanger et al., 2016).**

The exercise challenge test (ECT) is a common tool to assess exercise-induced asthma in school-aged children. Free running test is used for EIA diagnosis in school-aged children combined with measurements of spirometry **(Vilozni et al., 2007).**

Lipoxin A4 is a biological active lipooxygenase interaction product derived from arachidonic acid. Lipoxins and 15 epilipoxins are lipid mediators that modulate leucocyte trafficking and promote inflammation potential mediators or modulators of inflammation within the lungs **(Bhavsar et al., 2010).** Lipoxin A4 is a potent counter regulator signal for endogenous pro-inflammatory mediators including leukotriens and platelet activating

factor resulting in inhibition of leukocyte dependent inflammation **(Serhan et al., 2006).**

As lipoxins A4 are potent anti-inflammatory and several lipoxin forming multicellular interactions occur during strenuous, an urge is needed to evaluate the lipoxin A4 after exercise.