Relation between bronchial asthma, body composition and serum adiponectin level in obese asthmatic children

Thesis submitted for fulfillment of PhD in childhood studies

(Child Health and Nutrition)

Medical Studies of Children Department

By

Dina Ahmed Mohammed Salah Eldin El-fayoumy

M.Sc Pediatrics- Cairo University

Under Supervision of

Dr. Maysa Nasr Farid
Professor of pediatrics
Department of medical studies
Institute of postgraduate childhood studies

Dr. Lobna Sayed Sherif
Professor of child health
Department of child health
National research Centre

Dr. Nevine Elsayed Elhelaly
Professor of Pediatrics
Faculty of Medicine
Cairo University

Dr. Mona Hamed Ibrahim
Assistant Professor of Clinical & Chemical Pathology
National Research Centre

Institute of Postgraduate Childhood Studies

Ain Shams University

2016

بسم الله الرحمن الرحيم

"قَالُواْ سُبحَانَك لاَ عِلمَ لَنَاَ إِلّا
مَا عَلَّمَتَنَاَ إِنَّكَ أَنَتَ الَعَلِيمُ
الحَكِيمُ"

(صدق الله العظيم)
سورة البقرة (٣٢)

Acknowledgment

First of all, thanks to **ALLAH** the most generous and merciful for completing this work.

I would like to express my sincere thanks and deep gratitude to ***Prof. Dr. Maysa Nasr Farid***, Professor of pediatrics, Department of Medical Studies of Children, Institute of Postgraduate Childhood Studies, for her great support, kind guidance, meticulous revision and encouragement in performing this work.

I also wish to express my extreme appreciation, gratitude and respect to ***Prof. Dr. Lobna Sayed Sherif***, Professor of child health, Child Health department, National Research Centre, for her faithful supervision, valuable time, constructive guidance and real interest in the progress of this work.

Many sincere thanks to ***Prof. Dr. Nevine El Helaly, Professor*** of pediatrics, Faculty of Medicine, Cairo University, for her kind advice, help and support throughout this work.

My deepest thanks and gratitude to ***Prof. Dr. Tarek Salah***, Professor of child health, Child Health Department, National Research Centre, for his continuous support, guidance and encouragement.

I am also very thankful to **Ass**.***Prof. Dr. Mona Hamed***, Assistant Professor of clinical and chemical pathology, National Research Centre, who generously contributed to this work, and provided me with much support and guidance.

At last but not the least, I would like to express my profound gratitude and love to my whole family especially; my husband, for his great support and devoted care, my sons for their patience and love, my dear mother for her persistent faith and encouragement and my beloved father, may he rest in peace, who will always be my role model and inspiration.

Abstract

Asthma and obesity have serious health consequences and significant financial costs. The increase of asthma has paralleled the emerging obesity during the past decades. The ongoing epidemic of obesity in children has highlighted the importance of body composition for short term and long term health. Hence, components of body composition influence health outcomes, and their measurement is increasingly considered valuable in clinical practice.

Aim of the study: to evaluate the level of adiponectin as a hormone of energy metabolism in obese and non-obese asthmatic children, to investigate the association between serum adiponectin, CRP, IL- 6 levels and body composition parameters in asthmatic children, its effect on asthma severity and the clinical outcome and to emphasize on the bad effect of obesity on asthma and hence show the importance of weight loss for improvement of patients.

Subjects and Methods: the present study was conducted on 90 children. Their ages ranged from 7-12 years. Cases were divided into 2 groups; Group1: 30 non-obese asthmatic children. Group2: 30 obese asthmatic children. Another 30 apparently healthy children of matched age and sex as the control group, (Group 3). All cases were subjected to complete history taking and clinical examination. They comprised both males and females with an age range from 7-12 years. Anthropometric measurements (height & weight) were taken from the 3 groups as well as body composition parameters. Laboratory samples were collected from the 3 groups including: serum adiponectin, IL6 &CRP using the ELISA method.

Results: the obese asthmatic group showed highly statistically significant differences compared to the non-obese asthmatic group regarding: weight, BMI, Fat %, FM, FFM, IMP, TBW, BMR. The obese asthmatic group showed statistically significant differences compared to the

control regarding: weight, BMI, FM, FFM, IMP, TBW, BMR and fat%. The non-obese asthmatic group showed highly significant increase in serum IL6 and CRP compared to the control group. The obese asthmatic group showed highly significant increase in serum IL6 and CRP compared to the control group. Serum adiponectin level showed highly significant decrease in the obese asthmatic group compared to the control group. Serum adiponectin level showed highly significant decrease in the obese asthmatics both boys and girls compared to non-obese asthmatics. On the other hand, serum IL6 and CRP showed highly significant increase in the obese asthmatics compared to non-obese asthmatics.

Conclusion: Obesity aggravates the severity of asthma. Adiponectin markedly decreases in obese asthmatic children which plays a role in worsening asthma symptoms. CRP &IL6 increase sharing a big deal in the inflammation process. BMI, F%, FFM and IMP affect the level of adiponectin, CRP &IL6.

Key words: asthma, obesity, children, body composition, adiponectin, CRP, IL6

Contents

List of figures

List of figures

List of tables

List of abbreviations

WHO	World health organization
Th2	T helper 2 lymphocytes
VEGF	Vascular endothelial growth factor
GINA	Global initiative for asthma
COPD	Chronic obstructive pulmonary disease
IgE	Immunoglobulin E
RAST	Radioallergosorbent testing
ECG	Electrocardiograph
PFTs	Pulmonary function tests
FEV1	Forced expiratory volume in the 1st second
FEF25-75	Forced expiratory flow at 25-75% of vital capacity
PEFR	Peripheral expiratory flow rate
FVC	Forced vital capacity
HRCT	High resolution computed tomography
NHLBI	National Heart, Lung and Blood Institute
FDA	Food and Drug Administration
ICS	Inhaled corticosteroids
LABA	Long acting-β2 Agonists
IL-4	Interleukin 4
INF gamma	Interferon gamma
TNF	Tumor necrosis factor

BMI	Body mass index
CDC	Centre of disease control and prevention
IL-6	Interleukin-6
CRP	C reactive protein
TZD	Thiazolidinedione
CAD	Coronary artery disease
NF-kB	Nuclear factor kappa B
FM	Fat mass
FFM	Fat-free mass
F%	Percent body fat
TBW	Total body water
NHMRC	National Health and Medical Research Council
FRC	Functional residual capacity
ASM	Airway smooth muscle
NHLBI	National Heart, Lung, and Blood Institute
MAP	Mitogen-activated protein kinase
IMP	Impedance
BMR	Basal metabolic rate
NNI	National nutrition institute
hsCRP	High-sensitivity C reactive protein
TMB	Tetramethylbezidine
ROC	Receiver operating characteristic curve
SPSS	Statistical Package for Social Science

Introduction

Several epidemiological studies have shown that the prevalence of bronchial asthma and obesity is increasing concomitantly worldwide among children and young adults (**Ford, 2005**).

Asthma and obesity have serious health consequences and significant financial costs. The burden of obesity on pulmonary function in children is highlighted by the increased frequency of bronchial hyper-responsiveness, increased number of prescribed medications and inhaled corticosteroid (ICS) use, and reduced peak expiratory flow rate in overweight / obese asthmatic children compared to non-overweight asthmatic children. Excess body weight is also associated with an increase in the number of school days missed by asthmatic children and significantly reduced quality of life (**Van Gent et al, 2007**).

Asthma is a chronic inflammatory disease of the airways in which many 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. (**National Heart, Lung, and Blood Institute, Export panel report 3, 2008**).

For children and adolescents 2 to 18 years old, overweight is defined as a body mass index (BMI) at or above the 85th percentile and lower than the 95th percentile. Obesity is defined as a BMI at or above the 95th percentile for children of the same age and gender. (**Centers for Disease Control and Prevention. 2009**).

The increase of asthma has paralleled the emerging obesity during the past decades (**Chinn et al, 2001**). Several researches have concluded that there is a positive association between obesity and asthma (**Weiss, 2005, Beuther et al, 2006, Shore, 2007,**).Several mechanisms have been postulated (**Shore, 2006 and Shore, 2007**).

Firstly, genetic and environmental factors may increase the risk of obesity concurrently with asthma (**Hallstrand et al, 2005, Mai et al, 2007**). Secondly, obesity may increase the risk of asthma through its effects on other disease process, e.g. obesity is a risk factor for sleeping-disordered breathing and gastro-esophageal reflux disease (**Hampel et al 2004, Vazquez et al,2004**) and these two diseases are associated with an increased risk for asthma (**Sulit et al, 2005, Hancox et al, 2006**). Thirdly, morbid obesity can reduce lung volume and airway diameter and