

Impact of long term inhaled corticosteroids on anthropometric profile and serum cortisol level among Egyptian asthmatic children

THESIS

*Submitted for partial fulfillment for
The Master Degree in pediatrics*

By

Ahmed Mostafa Shaalan

M.B.B.CH.

National Research Centre

UNDERSUPERVISION

Prof .Dr. / Eman Ahmed Ihsan.

Professor of Pediatrics

Faculty of Medicine

Cairo University

Prof. Dr. / Nayera El-Morsi Hassan

Professor of Biological Anthropology

National Research Centre

Prof. Dr. / Hala Hamdi Shaaban

Professor of Pediatrics

Faculty of Medicine

Cairo University

Faculty of Medicine

Cairo University

2008

Abstract

We study anthropometric measurements and serum cortisol level in 63 Egyptian asthmatic children (40 boys and 23 girls), with an age range of 3-10 years (mean age 6.65 yr), did not receive systemic corticosteroids and not suffering from systemic chronic diseases, they were selected from the Allergy Clinic at the Children's Hospital, Cairo University.

We classified them in two groups, group1 (30 asthmatic patients on ICS) and group 2 (33 asthmatic patients not received ICS). We found that there is no significant difference in anthropometric measurements and serum cortisol level between the two groups; these results support the safety of ICS on growth. More over, we found that the height of group 2 (children not on ICS) are shorter than group 1 (patients on ICS) (significant $p = 0.013$).

Key Words :

adrenocorticotrophic hormone - adrenocorticotrophic hormone.

ACKNOWLEDGMENT

First and foremost *thanks to god* who granted me the ability to accomplish this work.

I would like to express my infinite gratitude and respect to my **Prof. Dr. Eman Ahmed Ihsan**, professor of pediatrics, Cairo University, for her continuous guidance and supervision, her kind encouragement and faithful support throughout the fulfillment of this work.

I would like to express my deep thanks and obligations to my **Prof. Dr. Nayera El morsi Hassan**, professor of biological anthropology, National Research Center, for her support, her continuous supervision and great help throughout the whole work.

I wish to thanks **Prof. Dr. Hala Hamdi Shaaban**, professor of pediatrics, Cairo University, for her constructive guidance, fruitful criticism, meticulous revisions of the whole text and constant help throughout every step of this work.

My sincere thanks go to assistant **Prof.Dr / Mona Anwar**. Assistant prof. of Biochemistry, National Research Center, for her support, her great help in analysis of samples and performing the analysis of the work.

Lastly no words could express my deepest unlimited indebtedness and love to my family, which offer me all help and encouragement that make this work possible

This work is humbly dedicated

To

MY FATHER

MY MOTHER

My Brothers

SARAH

&

My Wife

CONTENTS

	Page
Abbreviations	I
List of tables.....	V
List of figures.....	VII
 INTRODUCTION	 1
AIM OF THE WORK	3
REVIEW OF LITERATURE	4
SUBJECTS AND METHODS.....	85
RESULTS	92
DISCUSSION.....	107
SUMMARY AND CONCLUSIONS.....	113
RECOMMENEDATIONS.....	115
REFERANCES.....	116
APPENDIX.....	139
 ARABIC SUMMARY	

ABBREVIATIONS

ACTH: adrenocorticotrophic hormone.

ANOVA: analysis of variance.

B cells: B lymphocytes.

BDP: Beclonethasone dipropionate.

BHR: Bronchial hyperresponsiveness

BMI: Body mass index.

BMR: Basal metabolic rate.

BUD: Budesonide.

CAMP: Children asthma management program.

CBC: Complete blood count.

CC: Chest circumference.

CCs: corticosteroids.

Cm: centimeter.

d: day

DNA: Deoxyribonucleic acid.

e.g.: exempli gratia(for example).

ELISA: Enzyme Linked Immunosorbant Assay.

FDA: Food and drugs administration.

FEV1: forced expiratory volume in 1 second.

Fig.: figure.

FP: Fluticasone Propionate.

g: gram.

GCs: Glucocorticoids.

(GM-Csf): Granulocyte macrophage colony-stimulating factor

GR: Glucocorticoid Receptor.

HC: head circumference.

Hr: hour.

Ht: height.

i.e: id est. (that is)

ICS: Inhaled corticosteroids

IgE: Immunoglobulin E.

IGF-1: insulin growthn factor -1

IgG: immunoglobulin G.

IgM: immunoglobulin M.

IL-1: Interleukin 1

IL-5:Interleukin5

IL-6: Interleukin 6

ISAAC:International study of asthma and allergies in childhood.

IU: International unit.

K T cells: killer T cells.

Kg: kilo gram.

L: Liter.

LABA: Long-acting inhaled β_2 -agonists

LLL: Lower leg length.

Ltd.: Limited.

m²:square meter.

m: millimeter.

MAC: Mid arm circumference.

μg: microgram mg: milligram.

min: minute.

ml: milliliter.

Mm² : square millimeter.

mo :month.

N: number.

NCHS: National center for health statistics.

NS: Non significant

P: probability.

PEF: Peak expiratory flow.

PGF: Particularly peak expiratory flow.

r: correlation coefficient.

R: Receptors.

S: significant

SD: standard deviation.

SPSS: statistical package for social science.

SS: Subscabular skin –fold thickness.

Th: T helper.

TNF- α : tumor necrosis factor.

TS: triceps skin fold thickness.

UK: United Kingdom.

US: united state.

WHO: World health organization.

Wk: week.

Wt: weight.

Yr: year.

LIST OF TABLES

A-TABLES OF REVIEW page

TABLE (1)	risk factors and triggers of asthma	9,10
TABLE (2)	Mechanisms relating obesity to asthma.	12
TABLE (3)	GINA Classification of Asthma Severity By clinical features.....	21
TABLE (4)	Estimated Equipotent Daily Doses of Inhaled Glucocorticoids for Children.....	35
TABLE (5)	Daily medications used in different levels of asthma severity.....	40
TABLE (6)	Corticosteroid effects on airway Inflammation.....	48

B-TABLES OF RESULTS

TABLE (7)	Distribution of the study sample According to group.....	93
TABLE (8)	Distribution of the study sample According to age-group.....	94
TABLE (9)	Severity classification of asthmatic Children included in the study.....	95
TABLE (10)	Anthropometric measurements and serum Cortisol level of the study population.....	96
TABLE (11)	Duration of treatment with inhaled Corticosteroids (in month) in the study group.....	97

TABLE (12)	Dose of ICS (μ g) in children on ICS.....	99
TABLE (13)	Comparison of anthropometric Measurements and serum cortisol level Between the two groups of the study Sample among Egyptian asthmatic Children.....	100
TABLE (14)	Comparison of anthropometric Measurements and serum cortisol level Between the two SEX groups of the study Sample among Egyptian asthmatic Children	101
TABLE (15)	Comparison of anthropometric measurements and serum cortisol level in children on inhaled corticosteroid according to dose of ICS.....	102
TABLE (16):	Comparison of anthropometric measurements and serum cortisol level in children on inhaled corticosteroid according to duration of treatment with ICS.....	103
TABLE (17)	Comparison of anthropometric measurements and serum cortisol level according to severity of asthma.....	104
TABLE(18):	Correlation of anthropometric measurements and serum cortisol level ,dose of ICS and duration of treatment.....	106

LIST OF FIGURES

Figures of review	PAGE
FIGURE (1): the associations between atopy, asthma and BRH.	13
FIGURE (2): Management of asthma exacerbations in acute care setting.	33
FIGURE (3): Recommended medications by level Severity for children.	39
FIGURE (4): Corticosteroid action mechanisms.	47
FIGURE (5): Acute corticosteroid effects produced on the smooth muscle cell in airway mucosal blood vessels.	49
FIGURE (6): The fate of inhaled corticosteroids.	51
 Figures of results	
FIGURE (7): Sex distribution of the study population.	93
FIGURE (8): Severity classification of asthmatic children included in the study	95
FIGURE (9): Duration of treatment with inhaled corticosteroids (in months) in the study group.	97
FIGURE (10): Dose of ICS (in μg) in children on ICS.	99

INTRODUCTION

Bronchial asthma is a serious public health problem throughout the world, affecting people of all ages. When uncontrolled, asthma can place severe limits on daily life, and is sometimes fatal (*GINA, 2006*).

Asthma is the most common chronic disease of childhood; it is a worldwide problem that affects approximately 100 million people worldwide (*Kemp and Hartley, 2003*)

So, it is important to assess accurately the impact of such a wide spread illness and its treatment regarding efficacy and safety.

Inhaled corticosteroids are recommended as first line anti-inflammatory therapy for the treatment of asthma. Inhaled corticosteroids have been used for the treatment of asthma in children for more than 20 yr. During this time, a substantial number of studies have been performed evaluating the safety and efficacy of this therapy. Generally, the results have been reassuring. Inhaled corticosteroids have a marked effect on both the immediate and the long-term aims of asthma therapy, (*Pedersen S, 2001*)

However concern about the potential for systemic adverse events, including linear growth and suppression of adrenal glands, has resulted in reluctance of many physicians and parents to use ICS (*Altintas DU et al., 2005*).

Many physicians are concerned about the potential side effects. There are some reports about different side effects of inhaled steroids with different dosage and duration .However most of the studies focused on particularly growth, and serum cortisol level. Results on these side effects during corticosteroid therapy are conflicting. Several studies have reported poor correlation between corticosteroid-induced short term changes in the growth rate. On the other hand completely normal growth has been reported in children receiving ICS therapy. Serum cortisol level is another important point to discuss in children treated with ICS. Some investigators have found mild to moderate suppression of adrenal function while others have normal adrenal function (*Altintas DU et al., 2005*).

In this study we aimed to investigate the effect of long term inhaled steroids on linear growth, and serum cortisol level in asthmatic children.

AIM OF THE WORK

To investigate effect of long term inhaled corticosteroid on:

1-Serum cortisol level

2-Anthropometric profile in the form of:-

a- linear growth (height, sitting height)

B- Body weight.

C-Midarm, chest, waist, and hip circumferences.

d-Triceps,subscapular skin folds.

e-Body mass index.

3-To assess safety and efficacy of inhaled corticosteroids