Frequency of Small Bowel Bacterial Overgrowth (SBBO) in Asthmatic children on Inhaled Cortico Steroids (ICS)

Thesis

Submitted for Partial Fulfillment of Master Degree

in Pediatrics

By

Amr Faiz Hamed El-Zekyly

M.B.B.CH (2004)

Faculty of Medicine – Alexandria University

Under Supervision of

Prof. Yehia Mohamed El-Gamal

Professor of Pediatrics
Faculty of Medicine - Ain Shams University

Prof. Mostafa Abd El-Aziz El-Hodhod

Professor of Pediatrics
Faculty of Medicine - Ain Shams University

Dr. Zeinab Ebraheem Hasan

Assistant Professor of Pediatrics
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
2014

معدل حدوث النمو البكتيرى المتزايد في الأمعاء الدقيقة في الأطفال المصابين بالربو الشعبي والمعالجين بالكورتيزونات المستنشقة

رسالة

مقدمة تدوطئة للحصول على درجة الماجستير

في طب الأطفال

مقدمة من

الطبيب/ عمرو فايز حامد الزقيلي

بكالوريوس الطب والجراحة (٢٠٠٤)

كلية الطب - جامعة الإسكندرية

تحت إشراف

الأستاذ الدكتور/ يحيى محمد الجمل

أستاذ طب الأطفال

كلية الطب- جامعة عين شمس

الأستاذ الدكتور/ مصطفى عبد العزيز الهدهد

أستاذ طب الأطفال

كلية الطب — جامعة عين شمس

الدكتورة/ زينب ابراهيم حسن

أستاذ مساعد طب الأطفال

كلية الطب — جامعة عين شمس

كلية الطب

جامعة عين شمس

٢٠١٤

*First and foremost thanks to "**Allah**" who granted me the ability to accomplish this work, then to all the patients who cooperated with me.*

I would like to express my sincere appreciation and my deep gratitude to **Prof. Dr. Yehia Mohamed El-Gamal**, *Professor of pediatrics, Faculty of Medicine, Ain Shams University for his faithful supervision and guidance and his overwhelming kindness that has been of great help throughout this work.*

I am also deeply indebted to **Prof. Dr. Mostafa Abd El-Aziz El-Hodhod**, *Professor of pediatrics, Faculty of Medicine, Ain Shams University for his great support throughout the whole work.*

I would like to express my great thanks to **Dr. Zeinab Ebraheem Hasan**, *Assistant Professor of pediatrics, Faculty of Medicine, Ain Shams University, for her sincere support.*

Many thanks to my family for their meticulous support to complete this work.

Amr Faiz Hamed El-Zekyly

LIST OF CONTENTS

LIST OF ABBREVIATIONS

Abb.	Full term
µg	Microgram
AAAAI	American Academy of Allergy, Asthma and Immunology
AHRQ	Agency for Healthcare Research and Quality
B.bifidum	Bifidobacterium bifidum
BDP	Beclomethasone dipropionate
C. albicans	Candida albicans
C_{14} or $_{13}$	Carbon 14 or 13
CFU	Colony forming units
CH_4	Methane
CHO	Carbohydrates
CO_2	Carbon dioxide
FDA	Food and Drug Administration
DNA	Deoxyribonucleic acid
DTH	Delayed- type hypersensitivity
E.coli	Escherichia coli
EIA	Exercise induced asthma
FEV_1	Forced expiratory volume in 1 second
GBT	Glucose breath test
GERD	Gastro esophageal reflux disease

Abb.	Full term
GINA	Global initiative of asthma
GIT	Gastrointestinal tract
H	Hydrogen
H. pylori	Helicobacter pylori
H_2S	Hydrogen sulfide
HBT	Hydrogen breath test
HPA axis	Hypothalamic pituitary adrenal axis
IBD	Inflammatory bowel disease
IBS	Irritable bowel syndrome
ICS	Inhaled corticosteroids
IgA or IgE	Immunoglobulin A or E
IL	Interleukin
Kg	Kilograms
L.acidophilus	Lactobacillus acidophilus
LABA	Long acting β2 agonists
LBT	Lactulose breath test
LHBT	Lactulose hydrogen breath test
LTRA	Leukotriene receptor antagonists
Max	Maximum
MDI	Metered-dose inhaler
MMC	Migratory motor complex
NHLBI	National Heart Lung, Blood Institute

Abb.	Full term
NIH	National Institutes of Health
O_2	Oxygen
OCTT	Orocaecal transit time
PCO_2	Partial pressure of Carbone dioxide
PEF	Peak expiratory flow
PH	Power of hydrogen
PO_2	Partial pressure of oxygen
PPI	Proton pump inhibitor
PPM	Parts per millions
S.bouladii	Saccharomyces bouladii
S.cerevisiae	Saccharomyces cerevisiae
S.thermbophilus	Streptococcus thermbophilus
SABA	Short acting β2 agonists
SBBO	Small bowel bacterial overgrowth
SD	Standard deviation
SIBO	Small intestinal bacterial overgrowth
SLE	Systemic lupus erythematosus
TPN	Total parenteral nutrition
UC	Ulcerative colitis

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

Asthma is the most common chronic illness in childhood that affects 5% to 13% of the pediatric population **(Illi et al., 2006).**

Inhaled corticosteroids are the corner stone of long-term asthma management in children of all ages. Recent research efforts have focused on ways to improve inhalant drug delivery to lungs and minimize oral and systemic bioavailability so as to improve the therapeutic benefit: risk ratio **(McDaniel et al., 2006).**

The benefit of using aerosol drug therapy instead of oral or systemic therapy is to maximize the local effects in lung while minimizing systemic exposure and side effects. Nevertheless, systemic exposure occurs from aerosol deposited in the oropharynx that is swallowed, and the portion deposited in nose and lung that is absorbed directly into the circulation, bypassing hepatic first-pass metabolism. Thus, it is possible to see the same side effects with inhaled drugs as with the enteral or parenteral drugs, but at a significant reduced severity and/or frequency **(Geller, 2007).**

Inhaled corticosteroids (ICS) may have some adverse effects such as local candida infections. Although, there are

numerous studies on development of oropharyngeal candidiasis after inhaled corticosteroids (ICS) treatment. Yet, there are a restricted number of studies on prevalence of esophageal candidiasis due to its use **(Kanda et al., 2003).**

Small Bowel Bacterial Overgrowth(SBBO) in which colon-derived bacteria colonize the upper small bowel , is found in a wide variety of adult diseases associated with intestinal failure and dysfunction ,including short bowel syndrome and other conditions following massive bowel resection, dysmotility disorders, inflammatory bowel disease, malnutrition and immunodeficiency **(Ziegler and Cole, 2007)**

In 1989, **Denison and Wallerstedt reported** a 63-year-old man with SLE and selective IgA deficiency developed intractable diarrhea the day after treatment with prednisone, 50 mg daily, was started. The diarrhea was considered to be caused by bacterial overgrowth and was later successfully treated with doxycycline. Although IgA deficiency was a risk factor for bacterial overgrowth, another predisposing condition was necessary for development of this disorder and was supposed to be the high-dose treatment with corticosteroids.

So we thought that small bacterial bowel overgrowth (SBBO) would be a possible complication of inhaled corticosteroids (ICS).

To demonstrate the bacterial overgrowth to support the diagnosis of SBBO syndrome, direct culture of jejunal contents is considered the gold standard **(Bauer et al., 2000)**. However, this requires orointestinal intubation and proper specimen handling. Besides the fact that sampling aspirates is impractical, the scope of sampling leaves with isolated distal bacterial overgrowth undiagnosed **(Lin, 2004).**

SBBO syndrome was confirmed by bacteriologic analysis in 57% to 87% of patients with SBBO symptoms. Cultures from several different jejunal sites revealed that the overgrowth flora may be noncontinuous in the upper gastrointestinal tract, leading to false negatives when only 1 culture site is assessed. Cultures may be false negative; particularly in case of obligate anaerobes, false positives due to contamination mainly from the oral microbiota are believed to be common as well. Moreover, culturing reveals only a fraction (estimated at 20%) of microbiota compared with the molecular-based methods. Because of these disadvantages, noninvasive tests such as the lactulose breath test have been developed. The lactulose breath test relies on fermentation of lactulose by bacteria with release of hydrogen and methane. Hydrogen and methane are subsequently absorbed and expired. As lactulose is poorly absorbed, it is a suitable substrate for diagnosing bacterial overgrowth even in the distal small intestine **(Eckburg et al., 2005).**

AIM OF THE WORK

The objective of this study is to assess the presence of small bowel bacterial overgrowth (SBBO) in asthmatic pediatric patients receiving inhaled corticosteroids (ICS) managed at Allergy & Immunology unit and assessed in Gastroenterology unit, Pediatric Hospital, Ain Shams University.