

Effect of Zinc on Appetite and Growth in Primary Malnourished Egyptian Children

Thesis

Submitted for Partial Fulfillment of Master Degree
In Pediatrics

Presented by

Zaki Ahmed Zaki Emara

M.B.B.Ch, 2011

Faculty of Medicine, Ain Shams University

Under The Supervision of

Prof. Ehab Khairy Emam

Professor of Pediatrics

Faculty of Medicine- Ain Shams University

Prof. Mohamed Tarif Hamza

Professor of Clinical Pathology

Faculty of Medicine- Ain Shams University

Dr. Marian Girgis Rizk

Lecturer of Pediatrics

Faculty of Medicine- Ain Shams University

Faculty of Medicine

Ain Shams University

2018

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لَسْبِقَانِكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgment

*First and foremost, I feel always indebted to **ALLAH**, the Most Kind and Most Merciful.*

*I'd like to express my respectful thanks and profound gratitude to **Prof. Ehab Khairy Emam**, Professor of Pediatrics - Faculty of Medicine- Ain Shams University for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

*I am also delighted to express my deepest gratitude and thanks to **Prof. Mohamed Tarif Hamza**, Professor of Clinical Pathology, Faculty of Medicine, Ain Shams University, for his kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

*I am deeply thankful to **Dr. Marian Girgis Rizk**, Lecturer of Pediatrics, Faculty of Medicine, Ain Shams University, for her great help, active participation and guidance.*

I would like to express my hearty thanks to all my family for their support till this work was completed.

Last but not least my sincere thanks and appreciation to all patients participated in this study.

Zaki Ahmed Zaki Emara

Dedication

*Words fail to express my profound thanks and sincere gratitude to **Prof. Dr. Hamed Ahmed El-Khayat**, Professor of Pediatric, Faculty of Medicine – Ain Shams University, for his generous supervision, continuous encouragement, unlimited help and continuous guidance throughout this work,*



List of Contents

Title	Page No.
List of Tables	6
List of Figures.....	7
List of Abbreviations	9
Introduction	1
Aim of the Work	2
Review of Literature	
▪ Zinc	3
▪ Leptin and Satiety.....	13
▪ Relation between Zinc and Appetite, Zinc and Growth ..	27
Patients and Methods.....	38
Results	47
Discussion.....	66
Summary	73
Conclusion	76
Recommendations	77
References	78
Appendix	102
Arabic Summary	

List of Tables

Table No.	Title	Page No.
Table (1):	The Recommended Dietary Allowance (RDA) for Zinc.	6
Table (2):	The estimated amount of parenteral zinc required to maintain normal balance.	6
Table (3):	Descriptive data of the studied groups:	48
Table (4):	Comparative data between the test and control groups:.....	51
Table (5):	The difference between Serum Zinc level and Leptin Hormone level in the test and control groups before and after Zinc supplementation:.....	54
Table (6):	Changes in general examination and some lab investigation in case and control group before and after zinc supplementation or placebo.....	56
Table (7):	Changes in the control group before and after placebo administration:.....	57
Table (8):	Changes in the case group after Zinc administration:	58
Table (9):	Changes in the mean difference of CEBQ, Weight, Height, BMI, Mid upper arm circumference, serum Zinc level and Leptin Hormone level in test and control groups after Zn or placebo supplementation:.....	62

List of Figures

Fig. No.	Title	Page No.
Figure (1):	Structure of leptin hormone.....	17
Figure (2):	Receptor of leptin hormone.....	18
Figure (3):	Leptin dimerizes the leptin receptor (LepR) and activates a number of intracellular signaling molecules.	21
Figure (4):	Central LepRb expression sites and related neuronal circuits.....	23
Figure (5):	Gender distribution of the studied groups:.....	49
Figure (6):	Age data of the studied groups:	49
Figure (7):	Father education of the studied groups:.....	50
Figure (8):	Mother education of the studied groups:.....	50
Figure (9):	The difference between child eating behavior questionnaire (CEBQ) in the test and control groups.....	53
Figure (10):	The difference between body mass index (BMI) in the test and control groups.....	53
Figure (11):	The difference between Serum Zinc level in the test and control groups	55
Figure (12):	The difference between Leptin Hormone level in the test and control groups:.....	55
Figure (13):	Changes in the CEBQ in the case group after Zinc administration.....	59
Figure (14):	Changes in the body weight in the case group after Zinc administration.	59
Figure (15):	Changes in the height in the case group after Zinc administration.....	60
Figure (16):	Changes in the BMI in the case group after Zinc administration.....	60
Figure (17):	Changes in the serum Zinc level in the case group after Zinc administration.....	61
Figure (18):	Changes in the serum leptin hormone level in the case group after Zinc administration.....	61

List of Figures (Cont...)

Fig. No.	Title	Page No.
Figure (19):	Changes in the mean difference of CEBQ in cases and controls after Zn or placebo supplementation.....	63
Figure (20):	Changes in the mean difference of the weight in cases and controls after Zn or placebo supplementation	63
Figure (21):	Changes in the mean difference of height in cases and controls after Zn or placebo supplementation.....	64
Figure (22):	Changes in the mean difference of BMI in cases and controls after Zn or placebo supplementation.....	64
Figure (23):	Changes in the mean difference of serum level of Zinc in cases and controls after Zn or placebo supplementation.....	65
Figure (24):	Changes in the mean difference of leptin hormone level in cases and controls after Zn or placebo supplementation.....	65

List of Abbreviations

Abb.	Full term
<i>AgRP</i>	<i>Agouti-related-peptide</i>
<i>AN</i>	<i>Anorexia nervosa</i>
<i>ARC</i>	<i>Arcuate nucleus</i>
<i>BMI</i>	<i>Body mass index</i>
<i>CCK</i>	<i>Cholecystokinin</i>
<i>CeA</i>	<i>Amygdala</i>
<i>CEBQ</i>	<i>Child Eating Behavior Questionnaire</i>
<i>CGRP</i>	<i>Calcitonin gene-related peptide</i>
<i>DMH</i>	<i>Dorso-medial hypothalamus</i>
<i>EF</i>	<i>Enjoyment of Food</i>
<i>FDA</i>	<i>Food and Drug Administration</i>
<i>FR</i>	<i>Food Responsiveness</i>
<i>GABA</i>	<i>γ-aminobutyric acid</i>
<i>GABA</i>	<i>γ-aminobutyric acid</i>
<i>GIP</i>	<i>Gastric inhibitory peptide</i>
<i>GLP-1</i>	<i>Glucagon-like peptide-1</i>
<i>Glu</i>	<i>Glutamate</i>
<i>GRP</i>	<i>Gastrin-releasing polypeptide</i>
<i>HPC</i>	<i>Hippocampus</i>
<i>IFN-γ</i>	<i>Interferon gamma</i>
<i>IL-2</i>	<i>Interleukin 2</i>
<i>LHA</i>	<i>Lateral hypothalamic area</i>
<i>IPB</i>	<i>Lateral parabrachial nucleus</i>
<i>Nac</i>	<i>Nucleus accumbens</i>
<i>NTS</i>	<i>Nucleus of the solitary tract</i>
<i>Ob (Lep)</i>	<i>Ob for obese, Lep for leptin</i>
<i>ORS</i>	<i>Oral rehydration solution</i>
<i>PAG</i>	<i>Periaqueductal gray</i>
<i>POA</i>	<i>Prooptic area</i>

List of Abbreviations (cont...)

Abb.	Full term
<i>POMC</i>	<i>Proopiomelanocortin</i>
<i>PVN</i>	<i>Paraventricular nucleus</i>
<i>RDA</i>	<i>Recommended dietary allowance</i>
<i>RPa</i>	<i>Raphe pallidus</i>
<i>SCs</i>	<i>Sensory cortex</i>
<i>SNS</i>	<i>Sympathetic nervous system, DMV dorso-motor complex of vagus</i>
<i>SR</i>	<i>Slowness in Eating</i>
<i>THC</i>	<i>Tetrahydrocannabinol</i>
<i>TNF-α</i>	<i>Tumour necrosis factor α</i>
<i>UNICEF</i>	<i>United Nation's Children Fund</i>
<i>VTa</i>	<i>Ventral tegmental area</i>
<i>WHO</i>	<i>World Health Organization</i>
<i>Zn</i>	<i>Zinc</i>

INTRODUCTION

Zinc is an essential trace mineral for human nutrition; it is vital for several body functions, such as cell reproduction, growth, immunity, vision, and cognition. It plays an important role in metabolism, particularly as a cofactor of many enzymes, required for natural metabolic processes (*Fukada et al., 2011*).

There is an association between zinc deficiency and growth retardation, immune system disturbances, poor nutritional status, and high rates of infections (*Yang et al., 2012*).

Leptin is an adipocytokine that limits food intake and increases energy expenditure by acting on the hypothalamus (*Anshu et al., 2013*).

Studies are exploring the relationship between zinc and leptin demonstrate that zinc may critically impact leptin secretion (*Baltaci et al., 2005*).

Zinc has an important part in the regulation of nutrition. Marginal zinc deficiency is associated as much with decreased appetite as with low body mass and both of these negative situations can be corrected with zinc supplementation (*Jing et al., 2008*).

Stunting remains a major public health problem (*De Onis et al., 2012*).

Zinc is important for many biological functions, including reproduction, growth and development (*Maggini et al., 2010*).

AIM OF THE WORK

1. To determine Zinc status and Leptin hormone level in primary malnourished Egyptian infants and children.
2. To determine the effect of Zinc supplementation on serum levels of Leptin and Zinc and growth in primary malnourished Egyptian infants and children.
3. To assess the effect of zinc supplementation on Appetite and growth in primary malnourished Egyptian infants and children.

Chapter 1

ZINC

Introduction:

Zinc (Zn) is an essential trace mineral necessary for the proper functioning of multiple aspects of metabolism. It is present in numerous metalloenzymes, including major enzyme-classes (*Prasad, 2013*).

Zinc is the most universal of all trace elements involved in human metabolism. It is required for the normal structure and function of Zn containing enzymes, including those involved in gene expression, cell division, apoptosis, and synaptic signaling (*IZiNCG, 2004; Brown et al., 2004b*).

Zinc (Zn) is an essential metal involved in many biochemical processes, and its deficiency is associated with anorexia, weight loss, and growth retardation (*Mafrá et al., 2002; Jing et al., 2008*).

Imbalance or monotonous regimen and deficit of micronutrients can play an important role in taking insufficient food ingredients. Some selected micronutrients are shown to have the main roles in this regard like Iron, Zinc and magnesium (*Shamah-Levy et al., 2012*).

Prevalence of Zinc Deficiency:

Zinc deficiency is common in the developing countries (*Pinkaew et al., 2013; Akhtar, 2013*).

Zinc deficiency is very common world-wide but the actual prevalence figures are not known. WHO estimates that approximately 800, 000 deaths per year are related to zinc deficiency, and that over 50% of these are infants and children under 5 years of age. An estimate of overall prevalence of approximately 20% has been proposed (*Brown et al., 2004; Gibson, 2012*).

Inadequate zinc intakes were higher in countries with lower energy intakes, lower percentage energy from animal source foods, and diets with higher phytate: zinc molar ratio. The prevalence of stunting was positively associated with inadequate zinc intakes, although the prevalence of stunting was generally greater than that of inadequate zinc intake (*Wessells and Brown, 2012*).

Sources of zinc:

1) Food sources:

Yeast is a rich source of zinc, and this trace element is concentrated in the bran and germ of cereal grains. Animal protein by-products, such as fishmeal, are usually richer sources of the element than are plant protein supplements (*McDonald et al., 2010*).

2) Zinc Supplements:

A number of zinc supplements are available; including zinc acetate, zinc gluconate, zinc picolinate, and zinc sulfate. The percentage of elemental zinc varies by form. For example, approximately 23% of zinc sulfate consists of elemental zinc; thus, 220 mg of zinc sulfate contains 50 mg of elemental zinc. The elemental zinc content appears in the Supplement Facts panel on the supplement container (*Institute of Medicine, 2001*).

Zinc requirements and intakes:

Children consume around 5-8 mg/ day with intake rising with age to reach the adult levels of 8.6-14 mg/ day of zinc (*Hambidge, 2000*). National dietary surveys in the US estimated that the average dietary zinc intake was 9 mg/day for adult women and 13 mg/day for adult men (*Institute of Medicine, 2001*).

The US recommended dietary allowance (RDA) for zinc is listed by gender and age group in table (1).