Zinc Supplementation in the Treatment of Childhood Pneumonia in Hospitalized Children

Thesis for partial submission of Msc Pediatrics

By

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Dedication

To my Mother and my Father whom taught me the principles and patience

To my wife the angle of my life who gave me the smile during hard time
To all who sacrificed for me

Mostafa Badr

Acknowledgment

First and foremost, I feel always indebted to Allah, the most beneficent and merciful.

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Abstract

This randomized controlled trial was carried on 100 children with pneumonia admitted to Children's hospital, Cairo University. There were 47 male and 53 female. There age was between 2 and 60 months. They were divided into two groups, zinc group who receive elemental zinc (20 mg per day) for 14 days plus the hospital's standard antimicrobial management and non zinc group who received the hospital's standard antimicrobial management only. The outcome was reduction equivalent to 1 day hospital stay in zinc group.

Key words*:* Pneumonia, zinc supplementation, treatment, adjuvant therapy, Egypt

Contents

List of Tables

List of Figures

List of Abbreviations

AAP	American Academy of Pediatrics
ADH	Antidauritic hormone
AI	Adequate Intake
CAP	Community-acquired pneumonia
CMV	Cytomegalovirus
CRP	C-reactive protein
CSFII	Continuing Survey of Food Intakes of Individuals
CT	Computed tomography
DNA	Deoxy ribonucleic acid
DRIs	Dietary Reference Intakes
ELISA	Enzyme linked immunosorbent assay
ESR	Erythrocyte Sedimentation Rate
FiO2	Friction of inspired oxygen
FNB	Food and Nutrition Board
GAPP	Global Action Plan for the Prevention and Control of Pneumonia
HIV	Human Immunodeficiency virus
HSV	Herpes Simplex Virus
IFN-a	Interferon a
IFN-g	Interferon g
IL	Interleukin
IM	Intramuscular
IV	Intravenous

LRTI	Lower Respiratory tract Infection
NAS	National Academy of Sciences
NHANES	National Health and Nutrition Examination Survey
NK	Natural killer cells
PaCO2	Arterial Carbon Dioxide Tension
PCV	Heptavalent conjugated pneumococcal vaccine
PHA	Phytohemagglutination
PMNL's	Polymorphonuclear leukocytes
RDA	Recommended Dietary Allowance
RNA	Rib neuclec acid
RR	Respiratory rate
RSV	Respiratory syncytial virus
SaO_2	Oxygen saturation levels
Th1	T helper 1
Th2	T helper 2
TNF-a	Tumor necrosis factor a
UL	Tolerable Upper Intake Level
URTI	Upper respiratory tract infection
USA	United Stats of America
WHO	World Health Organization

Introduction

Pneumonia is the single largest cause of death in children worldwide. Pneumonia kills more than AIDS, malaria and measles combined. It was estimated that pneumonia is responsible for 10.000 deaths each year in children below the age of 5 years In Egypt, which represented 15% of the annual deaths in this age group ***(WHO, 2006).***

The central objective of the WHO's programme for the Control of Acute Respiratory Infections is to reduce the severity of and the mortality from pneumonia in young children. Case management intervention studies have demonstrated the substantial impact which can be achieved by treating children with inexpensive oral antibiotics ***(Sazawal, 2003).*** Preventive strategies can supplement case management efforts by reducing the incidence of pneumonia or severity of disease when it occurs ***(Kirkwood, 1995).*** Vaccination against pneumococci and *Haemophilus influenzae* type B have recently been shown to be effective though these may not be readily available in countries where they are most needed due to financial constraints ***(Peny et al., 2005).***

Zinc is an essential micronutrient whose deficiency has been linked to impairment of the nutritional rehabilitation following severe malnutrition in children. The biological role of zinc is extensive. Over 300 catalytically active zinc metalloenzymes from all the major enzyme classes and more than 2000 zinc dependant transcription factors have been recognised

(Vallee et al., 1993). Zinc has a regulatory role in gene expression, apoptosis and synaptic signalling. Zinc does not have any functional tissue reserves that can be released in deficient states like iron or vitamin A and thus, dietary zinc is crucial to meet the body's daily demand ***(Bhutta et al., 1999).*** It has, as such, an important role in immunological function, where rapid cell turnover is crucial ***(Fraker et al., 2000).***

Severe zinc deficiency depresses immune function , and even mild to moderate degrees of zinc deficiency can impair macrophage and neutrophils functions, natural killer cell activity and complement activity***(Wintergerst et al., 2007).***

The body requires zinc to develop and activate T-lymphocytes. Individuals with low zinc levels have shown reduced lymphocyte proliferation response to mitogens and other adverse alterations in immunity that can be corrected by zinc supplementation. These alterations in immune function might explain why low zinc status has been associated with increased susceptibility to ***pneumonia*** and other infections in children and the elderly in developing countries ***(Meydani, et al., 2007).***

Zinc deficiency is common in children of developing countries. Low protein diets contain low levels of zinc; protein value is a close correlate of zinc content. Current World Health Organisation (WHO, 2000) guidelines advise the use of zinc supplementation, 2mg/kg/day, for at least 2 weeks as part of the rehabilitation protocol.

Children with good zinc status may have a more robust immune response than those with poor zinc status ***(Shankar et al., 1998)***. Thus, our aim was to see whether zinc, along with antibiotics, would improve the outcome of pneumonia.

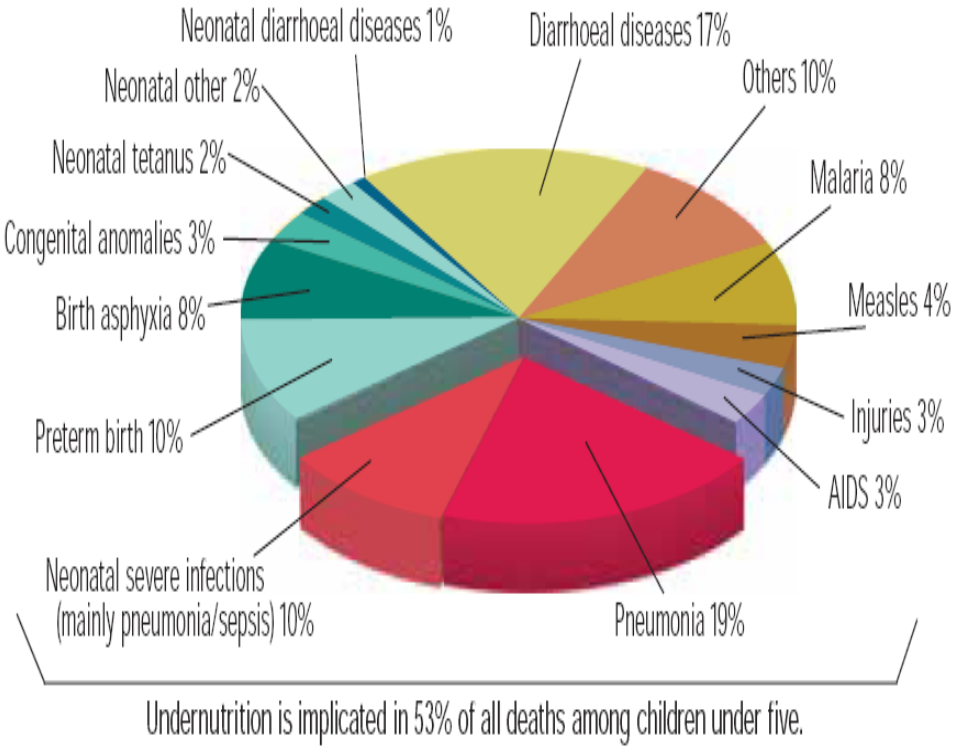
Aim of the Work

The central objective of the WHO's programme for the Control of Acute Respiratory Infections is to reduce the severity of and the mortality from pneumonia in young children. Case management intervention studies have demonstrated the substantial impact which can be achieved by treating children with inexpensive oral antibiotics.

The aim of this work is to evaluate the efficacy of zinc supplementation in the treatment of pneumonia in hospitalized Egyptian children who receive standard antimicrobial therapy. A hundred Children between 2 months and 5 years of age admitted to the pediatric wards of the hospital will be assessed. The zinc supplementation will be 20 mg elemental zinc per day, orally for 14 days. Thus, our aim was to see whether zinc, along with antibiotics, would improve the outcome of pneumonia and decrease the hospital stay.

Childhood Pneumonia

Pneumonia is the leading cause of pediatric morbidity and mortality. It was estimated that pneumonia is responsible for 2 million deaths each year in children below the age of 5 years, which represented 19% of the annual deaths in this age group ***(Bryce et al., 2005) Figure 1.*** Approximately 95% of the pneumonia-related deaths occur in developing countries; and the youngest age groups have the highest risk of death ***(Mulholland, 2003).***In Egypt, It was estimated that pneumonia is responsible for 10.000 deaths each year in children below the age of 5 years, which represented 15% of the annual deaths in this age group ***(WHO , 2006).***



(Bryce et al, 2005)

Figure 1 Pneumonia is the leading killer of children worldwide