Proton Magnetic Resonance Spectroscopy in Protein Energy Malnourished Infants

Thesis

Submitted for Partial Fulfillment of M.D Degree
In Pediatrics

By

Ahmed Naguib Ahmed
M.B., B.Ch., M. Sc.

Under Supervision of

Prof. Dr. / Sanaa Youssef Shaaban
Professor of Pediatrics
Faculty of Medicine – Ain Shams University

Prof. Dr./ Yasser Abdel Azzim Abbas
Professor of Radiology
Faculty of Medicine – Ain Shams University

Prof. Dr./ May Fouad Nassar
Professor of Pediatrics
Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
2009

List of contents **Page**

Acknowledgement

First of all, Praise be to **Allah** *the most merciful, the most mightiful.*

I would like to express my endless thanks and deepest appreciation to ***Prof. Dr. / Sanaa Youssef Shaaban****, Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for her valuable advice, insightful criticism and limitless patience. It has been an honour and a privilege working under her keen and meticulous supervision.*

I am deeply indebted to ***Prof. Dr./ Yasser Abdel Azzim Abbas****, Professor of Radiology, Faculty of Medicine – Ain Shams University, for his great help, continuous support and sincere advice during the practical part of this work..*

Endless thanks to ***Prof. Dr./ May Fouad Nassar****, Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for her great help, kind advice, meticulous supervision and*

persistent encouragement were important cornerstones of the present work.

I am greatly thankful to ***Prof. Abla Galal****. Professor of Child Health in National Reseach Centre, for her great help and effort in achieving this work.*

I wish to extend my thanks to my colleagues in the pediatric department for their cooperation and encouragement.

No words of gratitude would be enough to express what I owe my family. They have been there every step of the way and to them I dedicate every achievement.

Last but not least, all the thanks and prayers to the sick children by whom and for whom the present work was done.

Ahmed Naguib

List of Abbreviations

^{1}H	: Proton
^{1}HMRS	: Proton magnetic resonance spectroscopy
Ala	: Alanine
ALA	: α-linoic acid
ALT	: Alanine transaminase
AST	: Aspartate transaminase
BRS	: Behavior rating scale
BSID-II	: Bayley scales of infant development – second edition
CBC	: Complete blood count
Cho	: Choline
cMRI	: Conventional magnetic resonance image
Cr	: Creatine
CRP	: C-reactive protein
CSI	: Chemical shift image
CT	: Computed tomography
DHA	: Docosahexaenoic acid
EDTA	: Ethylene diamine tetracetic acid
EFAs	: Essential fatty acids
FAO	: Food and Agriculture Organization
FDA	: Food and drug administration
GER	: Gastroesophygeal reflux
Gln	: Glutamine
Glu	: Glutamate
Glx	: Glutamate and glutamine
Hb	: Hemoglobin
HC	: Head circumference
IBR	: Infant behavior recording
KWO	: Kwashiorkor
Lac	: Lactate

List of Abbreviations (Cont.)

Lip	: Lipids
MAC	: Mid arm circumference
MDI	: Mental developmental index
MRC	: Medical research council
MRI	: Magnetic resonance image
MRS	: Magnetic resonance spectroscopy
NAA	: N-acetyl aspartate.
NAAG	: N-acetylaspartylglutamate
PDI	: Psychomotor developmental index
PEM	: Protein-energy malnutrition
Ppm	: Part per million
PRESS	: Point resolved spectroscopy
PUFA	: Polyunsaturated fatty acids
SCU	: Severe childhood undernutrition
SES	: Socioeconomic scoring
SFT	: Skin fold thickness
SPECT	: Single photon emission computed tomography
Tc^{99m} HMPAO	: Technetium hexamethyl propyleneamineoxime
TLC	: Total leucocytic count

List of tables

Page

List of tables (Cont.)

Page

List of figures

Page

List of figures (Cont.)

Page

INTRODUCTION

Nutrition plays a critical role in prenatal and early postnatal development of the brain at different levels including structural, chemical and functional levels ***(Guesry, 1998)***.

Moderate to severe periods of malnutrition prior to the 1st two years of life are known to be associated with delay in cognitive development and poor scholastic performance in children ***(Galler and Ross, 1993)***.

The rapidly developing brain is more vulnerable to nutrient insufficiency. Certain nutrients have greater effects on brain development than do others. These include protein, energy, certain fats, iron, zinc, copper, iodine, selenium, vitamin A, choline, and folate. The effect of any nutrient deficiency or overabundance on brain development will be governed by the principle of timing, dose, and duration ***(Georgieff, 2007).***

Severe, moderate and even mild malnutrition have been shown to have permanent effect on brain development ***(Wachs, 1995)***.

Early studies done by ***Gunston et al. (1992)***, reported that the consequences of severe protein energy malnutrition (PEM) on the developing brain were still ill defined. Imaging studies were done to explore the underlying abnormalities in PEM infants.

Shaaban (1977) had used pneumoencephalographic study for PEM infants and concluded that the small head circumference in her patients was due to atrophy of cerebral cortex and subcortex with some dilatation of the ventricles and enlargement of subarachnoid spaces of both marasmic and kwashiorkor infants. The study also reported that severe malnutrition when started at an early age regardless its type threatened the brain growth and the earlier the onset, the severer the insult to the brain. With advances of imaging studies, ***Household and de Villiers (1987)*** reported cerebral atropy in children with kwashiorkor (KWO) using computerized tomography (CT) study.

Later on, magnetic redonance imaging (MRI) study done by ***Gunston et al. (1992)*** and revealed cerebral shrinkage in children with KWO yet the underlying reason for cerebral shrinkage was unclear.

In trials to reach to the functional changes or the underlying pathology in the brain of KWO infants, ***Mohamed (1996)*** showed brain atrophy and significant decrease in cerebral blood flow (especially affecting the frontal lobes and basal ganglia) which was correlated positively with the severity of the condition through CT and single photon emission computerized tomography (SPECT) study using technitium (Tc^{99m}).

In the last years, magnetic resonant spectroscopy has been developed as a direct medical application of nuclear

magnetic resonant system. It determines non-invasively the presence and the quantity of various compounds in tissues. It has been used in patients with refractory epilepsy and brain tumours referred to surgery ***(Frahm and Hanefeld, 1997)***.

There is evidence that the concentration of normal metabolites in the brain varies with age, this variation is more noticeable during the first three years of life. The most striking variation is an increase in N. acetyl aspartate (NAA)/creatine (Cr) ratio and decrease in choline (Cho)/creatine ratio as the brain matures. These changes may reflect neuronal maturation and an increase in number of axons, dendrites and synapses ***(Stoll et al., 1995)***.

NAA is a neuronal marker and its concentration will decrease with many insults to the brain. Whereas choline is a constituent of the phospholipid metabolism of cell membrane and reflects membrane turnover and it is the precursor of acetyl choline (A.Ch) and phosphatidylglycerol. The former is a critical neurotransmitter involved in memory, cognition and mood, the latter is used to build up cell membranes and low choline has been observed in hepatic encephalophy also low intake of choline can modulate cerebral choline level. Whereas creatine plays a role in maintaining energy dependent systems in brain cells ***(Stoll et al., 1995)***.

AIM OF THE WORK

This study was designed to assess the potential role of proton MRS in detecting the metabolic changes in the brain of PEM infants.

Protein Energy Malnutrition

Protein-energy malnutrition (PEM) continues to affect millions of human beings in developing countries. Children suffer most from the shortage of nutrients because at early ages malnutrition has an important impact on the central nervous system. The changes that malnutrition triggers in the brains of these children will have severe consequences on their development and learning abilities ***(Cornelio-Nieto, 2007).***

Malnutrition remains one of the most common causes of morbidity and mortality among infants and children throughout the world. The earlier the onset, the more the incidence of permanent impairment of brain development ***(WHO, 1999)***.

The long-term effects of nutritional deficiencies in early life depend on the severity and duration of the deficiency, the stage of the children's development, the biological condition of the children and the socio-cultural context ***(Grantham-McGregor, 2000)***.

The World Health Organization (WHO) defines malnutrition as "the cellular imbalance between the supply of nutrients and energy and the body's demand for them to ensure growth, maintenance, and specific functions" ***(Onis et al., 1993).*** The term protein-energy malnutrition (PEM) applies to a group of related disorders that include marasmus, kwashiorkor, and intermediate states of marasmus-kwashiorkor. The term