Assessment of Serum level of Zinc and Copper in a Sample of Egyptian Children with Phenylketonuria

Thesis

Submitted for the fulfillment of the M.SC. Degree in Childhood Studies (Child health and Nutrition).

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2011

Acknowledgement

First and foremost , thanks to ALLAH ,to whom I relate every success in achieving any work in my life.

I would like to express my sincere appreciation and deepest gratitude to Prof. Dr Randa Kamal, Prof. of pediatrics, for her valuable supervision and advice in initiation , progress and completion of this work.

I am greatly indebted to Pro Dr. Laila Effat, Prof of molecular genetics for her support and sincere cooperation allover the study.

My deepest thanks also to Prof.Dr. Maha Saber, Prof of child health for her continuous support and advices.

Special thanks and deep appreciation to Dr. Hala Koura, who has provided her support,help and encouragement throughout the whole study.

My deepest thanks also to Prof.Dr. Hanaa El Sherif, prof of biochemistry, for her help and cooperation.

I wish to express my thanks to the patients and their parents for their cooperation.

I wish to record my appreciation to all members of my family whose love and encouragement have been my inspiration to accomplish this work.

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2011

List of abbreviations

AR	Autosomal recessive.
BBB	Blood brain barrier.
Cu	Copper.
CVD	Cardiovascular diseases
DHA	Docosahexanoic acid
EEG	Electroencephalogram
HIAA	Hydroxy indolacetic acid
HPA	Hyperphenylalaninemia
HVA	Homovanillic acid
IEMS	Inborn error of metabolism
IQ	Intelligence quotient
IQR	Interquartile range
LCPUFA	Long chain polyunsaturated fatty acids
LDL	Low density lipoprotein
LNAAs	Large neutral amino acids
MRI	Magnetic resonance image
PAH	Phenylalanine hydroxylase
Phe	Phenylalanine

PKU	Phenylketonuria
RDA	Recommended dietary allowance
SD	Standard deviation
Trp	Tryptophan
Tyr	Tyrosine
Zn	Zinc

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Abstract

Background: Phenylketonuria is an autosomal recessive metabolic disorder in which the essential amino acid phenylalanine (Phe) cannot be converted into tyrosine, leading to the accumulation of toxic metabolites. In the absence of treatment, the clinical manifestations of PKU include mental retardation as well as behavioral and dermatological problems. Consequently, the dietary regimen of PKU depends mainly on a protein restricted diet together with phenylalanine free milk formula.

The low ingestion of proteins with a high biologic value and the predominance of vegetable-origin foods containing fibers, phytates, oxalates, and tannins in the diet decrease the bioavailability of many nutrients.

Some studies reported low serum level of zinc and copper in phenylketonuric children and adolescents.

Objectives: This study aimed to assess serum levels of zinc and copper in a group of Egyptian children with phenylketonuria, and to determine the effects of diet on blood phenylalanine levels, IQ and neurological functions of this group.

Methods: The study was conducted on 31 children suffering from phenylketonuria (19 males and 12 females).Their age ranged from 3 to 18 years with a mean age of 11± 4.5.

Full history taking, thorough clinical examination, assessment of serum levels of zinc and copper, plasma phe and IQ assessment were done for all studied patients.

Results: The overall consanguinity rate recorded in the current study was 90.3% and family history of PKU was present in 64.5% of cases. Different degrees of mental retardation were reported in 50% of pku cases enrolled in the current study. The IQ of the studied sample ranged between 30 and 90 with mean value of 68±16. The median value of phe was 12 mg ⁄ dl , with IQR (4-15).The mean value of zinc concentration in the studied groups was 105.9 ± 29.9 microgram .while the mean

value of copper was 88.8 ± 20.4. In the current study serum levels of zinc and copper were within normal ranges in all of the studied patients.

Non compliant children had significant higher phenylalanine and lower IQ than compliant children. There was significant negative correlation between IQ and age of start of diet therapy, age of sitting, standing, walking, mother recognition and speaking. Significant negative correlation was found between plasma levels of phenylalanine and weight, height and darkness of hair color, while there was significant positive correlation between plasma levels of phe and serum levels of Cu. Cu and IQ were significantly higher in children who received early diet therapy.

Conclusion: Serum levels of Zinc and copper were within the normal ranges in the studied patients with PKU. Children who were compliant to diet therapy had significant lower phenylalanine levels and higher IQ than non compliant children , and there were significant negative correlation between IQ and ages of start of diet therapy, age of sitting, standing, walking, mother recognition and speaking .

Keywords: phenylketonuria, zinc, copper.

Introduction

iIntroduction

Phenylketonuria (PKU) is an autosomal recessive genetic disorder characterized by a deficiency in the enzyme phenylalanine hydroxylase (PAH). This enzyme is necessary to metabolize the amino acid phenylalanine to the amino acid tyrosine. When PAH is deficient, phenylalanine accumulates and is converted into phenylpyruvate (also known as phenylketone), which is detected in the urine ***(Scriver et al, 1998).***

If Left untreated, this condition can cause problems with brain development, leading to progressive mental retardation and seizures. However, PKU is one of the few genetic diseases that can be controlled by diet if early diagnosis and early introduction of diet therapy occurred. A diet low in phenylalanine and high in tyrosine can be a very effective treatment ***(Burgard et al, 1997).***

Untreated children are normal at birth, but fail to attain early developmental milestones, develop microcephaly, and demonstrate progressive impairment of cerebral function. Hyperactivity, EEG abnormalities, seizures, and severe learning disability are major clinical problems later in life. A "musty" odor of skin, hair, sweat and urine (due to phenylacetate accumulation); and a tendency to hypopigmentation and eczema are also observed. In contrast, affected children who are diagnosed early enough and treated by eating a special diet low in phenylalanine are less likely to develop neurological problems or mental retardation***(Beblo et al 2007).***

Dietary therapy is the predominant treatment for phenylketonuria (PKU). To maintain the level of phenylalanine within a narrow range (Since phenylalanine is necessary for the synthesis of many proteins, it is required but its level must be strictly controlled), the recommended diet is a low protein diet that excludes animal products (because of their high phenylalanine content) and includes controlled

amounts of cereal, fruit, and vegetables, in addition to protein supplementation with phenylalanine-free metabolic formulas ***(Mira et al, 2000).***

Trace elements are essential in the daily diet because they have various important functions. Protein and carbohydrate malnutrition can develop due to deficiencies in micronutrients like vitamins and in trace elements like zinc and copper which are involved in multiple biological processes as constituents of enzyme systems including superoxide dismutase, oxidoreductase, and glutathione peroxidase. Blood levels of zinc and copper have been monitored in several experimental nutrition studies and are widely used to determine the presence of the deficiency states or toxicity ***(Cunninngham, 2005).***

Zinc is an essential mineral found in almost every cell and approximately 100 enzymes contain this element for biochemical reactions in the body and its deficiency occurs due to inadequate intake, decreased absorption or when there is increased loss of it from the body, or when the body's requirement for it increases ***(Anug et al 2006).***

Copper can affect different target organs such as bone marrow, the central and peripheral nervous systems and the cardiovascular system ***(Spinazzi et al, 2007).***

The low ingestion of proteins with a high biologic value and the predominance of vegetable-origin foods containing fibers, phytates, oxalates, and tannins in the diet decrease the bioavailability of many nutrients ***(Acosta et al ,1996).***

Some studies reported low serum level of zinc and copper in phenylketonuric children and adolescents ***(Anderson et al 2002 and Barreto et al 2008).***