Hair Magnesium Content and its Relation to Serum Magnesium Level in Children with Idiopathic Epilepsy

Thesis

Submitted for Partial Fulfillment of Master Degree in Pediatrics

By

Alaa Rabie Abdel Baset Mahmoud

MB.B.Ch, (2010)

Faculty of Medicine, Ain Shams University

Supervised By

Prof. Dr. Hamed Mahmoud Shatla

Professor of Pediatrics

Faculty of Medicine, Ain Shams University

Dr. Mariam Fathy Abdel Maksoud

Lecturer of Clinical Pathology

Faculty of Medicine, Ain Shams University

Dr. Raghda Mohamed Hesham Zaitoun

Lecturer of Pediatrics

Faculty of Medicine, Ain Shams University

Faculty of Medicine

Ain Shams University

2019

Acknowledgement

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

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

Sincere and special thanks go out to **Dr. Mariam Fathy Abdel Maksoud,** *Lecturer of Clinical Pathology, Faculty of Medicine– Ain Shams University, for her unexampled kindness and support.*

I am also delighted to express my deepest gratitude and thanks to **Dr. Raghda Mohamed Hesham Zaitoun,** *Lecturer of Pediatrics, Faculty of Medicine, Ain Shams University, for her kind care, infinite effort, continuous supervision, valuable instructions, constant and great assistance throughout this work.*

I would like to heartily express my thanks to ***my family, friends*** *and* ***colleagues*** *for their support till this work was completed. My sincere thanks and appreciation to all our patients who participated in this study, in the hopes that this work will help us serve them, and all other patients, with the best level of care possible.*

May God bless them all

Alaa Rabie

Contents

List of Abbreviations

Abb.	Full term
ACTH	Adrenocorticotropic hormone
ADEAF	Autosomal –dominant epilepsy with auditory features
ADHD	Attention deficit hyperactivity disorder
ADNFLE	Autosomal dominant nocturnal frontal lobe epilepsy
AED	Anti-epileptic drug
AMPA	α-amino-3-hydroxy-5-methyl-4-isoxazolepropioniaacid
AMPAR	α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptor
ASD	Autism spectrum disorders
BCECTS	Benign epilepsy of childhood with centro-temporal spike
BECTS	Benign epilepsy with Centro temporal spikes
BECTS	Benign epilepsy with centrotemporal spikes
BFIS	Benign familial infantile seizures
BFNE	Benign familial neonatal epilepsy
BNFIS	Benign non familial infantile seizures
BNS	Benign neonatal seizures
BOHB	Acetoacetate, beta-OH-butyrate
C	Chi Square test of significance
CAE	Childhood absence epilepsy
CBZ	Carbamazepine
Cm	Centimeter
COE-G	Childhood occipital epilepsy of Gastaut
CSWS	Continuous spike and wave during sleep

Abb.	Full term
CT	Computed tomography
EEG	Electroencephalogram
EGTCO	Epilepsy with generalized tonic-clonic seizures alone
EIEE	Early Infantile Epileptic Encephalopathy
EMA	Epilepsy with myoclonic absences
EMA	Epilepsy with myoclonic absences
EME	Early myoclonic encephalopathy
ER	Endoplasmic reticulum
F	Fisher's exact test of significance
FMRI	Functional magnetic resonance imaging
fMRI	Functional magnetic resonance imaging
FS	Febrile seizures
G	Gram
GABA	Gamma amino butyric acid
GEFS+	Generalized Epilepsy with Febrile seizures plus
GLUT 1	Glucose transporter deficiency
GTCS	Generalized tonic clonic seizures
H.C	Head circumference
ILAE	International League against Epilepsy
IQR	Interquartile range
IS	Infantile Spasms
IVIG	Intravenous immunoglobulins
JAE	Juvenile absence epilepsy
JME	Juvenile myoclonic epilepsy
Kg	Kilograms
KGD	Ketogenic Diet

Abb.	Full term
LEV	Levetirectam
LGS	Lennox-Gastaut syndrome
LKS	Landau-kleffner syndrome
MAE	Myoclonic astatic epilepsy
MAS	Myoclonic astatic seizures
MEI	Myoclonic epilepsy in infancy
Mg	Magnesium
Ml	Milliliter
MMP	Matrix metalloproteinase
MMPEI	Malignant migrating partial epilepsy of infancy
MRI	Magnetic resonance imaging
MRS	Magnetic resonance spectroscopy
MSI	Magnetic source imaging
MTLE	Mesial temporal lobe epilepsy
N	Number
NMDA	N-Methyl- d-aspartic acid or N-Methyl- d-aspartate
NMDAR	N-methyl-D-aspartate receptor
NS	Non significant
OXBZ	Oxcarbazepine
PET	Positron emission tomography
PHB	Phenobarbital
PHD	Pyruvate dehydrogenase deficiency
PME	Progressive myoclonus epilepsies
RDA	Recommended daily allowance
S	Significant
SD	Standard deviation

Abb.	Full term
SMEI	Severe myoclonic epilepsy of infancy
SPECT	Single photon emission computerized tomography
SUDEP	Sudden unexpected death in epilepsy
SW	Spike and wave discharges
TA	Typical absence
TPM	Topiramate
Ug	Micrograme
VGCC	Voltage-gated Ca2+ channels
VNS	Vagus Nerve Stimulator
VPA	Valproate

List of Tables

List of Figures

Hair Magnesium Content and its Relation to Serum Magnesium Level in Children with Idiopathic Epilepsy

Abstract

Objective: to measure the level of hair magnesium, comparing it to that in serum, in patients with epilepsy and compare them to the levels found in non-epileptic age and gender matched children.

Methods: An observational cross-sectional study including 50 children with idiopathic epilepsy and 100 non-epileptic age and gender matched control subjects. Cases were subjected to full history taking, examination and measurements of serum and hair levels of magnesium, control subjects only had their serum and hair level of magnesium measured as for the cases.

Results: The mean serum magnesium was 29.11 ± 13.42 ug/ml for cases and 27.67 ± 7.24 ug/ml for controls and the median hair level of magnesium was 42.22 ug/g with IQR of 25.9 - 56.82 for cases and 38.6 ug/g with IQR of 25.21 - 61.25 for controls. No statistically significant difference was observed between both groups as regards either serum or hair magnesium levels. No statistically significant correlation was observed between either hair or serum levels of magnesium and seizure characteristics though the correlations were nearing statistical significance for the hair magnesium content.

Conclusion: Hair magnesium level may be better correlated to seizure characteristics and control than serum levels in patients with epilepsy and may be a better indicator of body content of the mineral than serum.

Key words: Hair Magnesium, Serum Magnesium Level, Idiopathic Epilepsy**.**

Introduction

Epilepsy is a disorder of the brain caused by abnormal excessive or synchronous neuronal activity in the brain which leads to the generation of epileptic seizures. It is clinically defined by any of the conditions (1) at least 2 unprovoked seizures occurring >24 hrs apart or (2) one unprovoked seizures and probability of further seizures similar to general recurrence risk after 2 unprovoked seizures or (3) epilepsy syndrome ***(Fisher et al., 2014).***

Causes of epilepsy are divided into 4 main categories: (1) genetic such as Specific genetic epilepsy syndromes, genetic and chromosomal developmental encephalopathies, (2) structural such as brain malformation, brain tumors, (3)metabolic such as inborn errors of metabolism, alteration in blood and serum trace elements levels, (4) and unknown causes ***(Berg et al., 2010)*** .

The equilibrium of trace elements is essential for a healthy nervous system as they activate specific enzymes that act as antioxidants ***(Hayashi, 2009).***

Magnesium (Mg) is an essential element having a role in neuronal excitability. It helps in slowing the electric discharge as well as its spread in the brain. Hence depletion of magnesium can lead to hyper excitability of neurons

(Zhou, 2014). Low Mg can reduce surface charge of neuronal membrane, thereby increasing neuronal hyper excitability ***(Isaev et al., 2012).***

Magnesium is a potential modulator of seizure activity because of its ability to antagonize the excitatory calcium influx through NMDA receptor ***(Sinert et al., 2007)*** and it was also demonstrated that low levels of magnesium can increase the frequency of seizures in the patients with refractory epilepsy that is considered to be the most important risk factor for occurrence of sudden unexpected death in epilepsy (SUDEP) ***(Surges et al., 2009).***

To assess the mineral status, mineral concentrations are determined in various biological materials (e.g. serum, urine). Some authors believe that head hair may be a good mineral body biomarker and it provides retrospective information on the exposure and nutritional status of individuals ***(Gellein et al., 2008).***

Aim of the Work

The aim of the work is to:

1) Measure the levels of hair and serum magnesium in patients with epilepsy; comparing them to the levels found in non-epileptic age and gender matched controls.
2) Correlate hair to serum levels of magnesium in epileptic patients and in healthy controls.
3) Explore the potential impact of magnesium status on disease characteristics in epileptic patients.

Chapter (1):

Epilepsy

Disorder of the brain characterized by an enduring predisposition to generate seizures and by the neurobiological, cognitive psychologic, and social consequences of this condition. The clinical diagnosis of epilepsy usually requires the occurrence of at least 1 unprovoked epileptic seizure with either a second such seizure or enough EEG and clinical information to convincingly demonstrate an enduring predisposition to develop recurrences. For epidemiologic and commonly for clinical purposes, epilepsy is considered to be present when 2 or more unprovoked seizures occur in a time frame of longer than 24 hr ***(Berg et al., 2010)***.

Epidemiology

Incidence and Prevalence

Epilepsy is one of the most common chronic neurological disorders. Approximately 65 million people worldwide have epilepsy. In developed countries, the annual incidence of epilepsy is nearly 50 per 100,000 population (range 40–70 per 100,000/year) but is generally higher in resource-poor countries, between 100 and 109 per 100,000/year ***(Thurman et al., 2011).*** The prevalence of