

**Serum Level of Vitamin E in Children
With Intractable Epilepsy on
Ketogenic Diet**

Thesis

*Submitted for Partial Fulfillment of the Master
Degree in Pediatrics*

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2017

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لسببائك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgment

*First thanks to ALLAH to whom I relate any success
in my life*

I sincerely dedicate this research and thesis to Prof. Neveen Tawakol Younis Professor of Pediatrics Faculty of Medicine - Ain Shams Univerisity for her meticulous supervision, kind guidance, valuable instructions and generous help.

I wish to express my deepest thanks and appreciation to Dr. Yasmin Gamal Abdo El-Gendy Lecturer of Pediatrics Faculty of Medicine - Ain Shams University, for her kind advices, valuable instructions, encouragement and great help throughout the course of this study.

Special thanks are due to Dr. Shaymaa Maher Deifalla Lecturer of Pediatrics Faculty of medicine - Ain Shams University, for her sincere efforts, encouragement and I learned from working with her how to be an honourable caring doctor.

I have no words to express my gratitude to my parents and my husband for being my backbone in life and without their continuous support in hard times and caring environment that they provide me with I would not achieve my goals in life.

Rasha Ahmed Abd El-Fattah

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List of Abbreviations

Abb.	Full term
ACTH	Adrenocorticotropic hormone
ADHD.....	Attention-deficit hyperactivity disorder
AEDs	Antiepileptic drugs
AI.....	Adequate intake
APC	antigen-presenting cells
ASD	Autism spectrum disorder
ATP	Adenosine triphosphate
BHB.....	Beta-hydroxybutyrate
BMI	Body mass index
BNF	British National Formulary
CBC	Complete blood count
CBZ	Carbamazepine
CDC.....	Center for Disease Control
CPT.....	Carnitine Palmitoyl Transferase
DNA	Deoxyribonucleic acid
DRE	Drug Resistant Epilepsy
EEG	Electroencephalogram
EFSA	European Food Safety Authority
ELISA.....	Enzyme-Linked ImmunoSorbent Assay
FDA	Food and Drug Administration
GI.....	Gastrointestinal
GIT	Gastrointestinal tract
GLUT1	Glucose transporter 1
GST	Glutathione S-transferase
GTC	Generalized tonic clonic

List of Abbreviations

Abb.	Full term
Hb	Hemoglobin
HC	head circumference
HDL	High density lipoproteins
HRP	Horseradish Peroxidase
Ht	Height
IU	International unit
IV	Intravenous
KBs	Ketone bodies
KD	Ketogenic diet
LCT	Long chain triglycerides
LDL	Low-density lipoproteins
LGIT	Low Glycemic Index Diet Treatment
LINAC	Linear particle accelerator
MAC	Mid-arm circumference
MAD	Modified Atkins Diet
MCT	Medium chain triglycerides
MRI	Magnetic resonance imaging
NADPH	Nicotinamide adenine dinucleotide phosphate
NHS3	National Health Seizure Severity Scale
PDHD	Pyruvate dehydrogenase deficiency
P-gp	P-glycoprotein
PUFA	Polyunsaturated fatty acids
RBC	Red blood cell
RDA	Recommended Daily Allowance
SD	Standard deviation

List of Abbreviations

Abb.	Full term
SPSS	Statistical Program for Social Science
TMB	Tetramethyl benzidine
UK	United Kingdom
USNIH	United States National Institutes of Health
VLBW	Very low birth weight
VLDLs	Very low density lipoproteins
VNS	Vagus nerve stimulation
VPA	Valproatic acid
WBCs	White blood cells
WHO	World Health Organization
Wt	Weight

Abstract

The ketogenic diet continues to be one of the most effective therapies for drug-resistant epilepsy in the pediatric population. The restricted food choices of a ketogenic diet raise concerns about possible deficiencies in vitamin and mineral intake. Our aim was to detect symptoms and signs of vitamin E deficiency and measuring its serum level in a cohort of patients with drug resistant epilepsy before commencing ketogenic diet and 3 months later.

Subjects and Methods:

Twenty patients with drug resistant epilepsy candidates for ketogenic diet were evaluated through the first 3 months of commencing the classic ketogenic diet therapy (4 patients) or MAD (16 patients) tailored according to local Egyptian ingredients.

Dietary assessment was done with calculation of calories utilized per day and amount of vitamin E in patient's diet. Seizure frequency/day, Chalfont seizure severity scale, weight, length, serum level of vitamin E and lipid profile were assessed upon enrollment and after 3 months.

Results:

Our 20 patients included 10 males and 10 females with mean age of 3.15 ± 2.92 years. The etiology of epilepsy was: Structural/Metabolic(10); Malformation of cortical development(5), Acquired perinatal insults(5). Genetic (6), Unknown etiology(4). 50% had GTC, 25% had focal seizures, 15% had infantile spasms and 10% had myoclonic seizures.

Chalfont scores and seizure frequency significantly decreased. The patient's weight and length z-scores increased non significantly. Serum vitamin E levels decreased significantly. Total cholesterol, triglycerides and LDL serum levels significantly increased.

Conclusion:

KD is an effective therapy for drug resistant epilepsy with improvement in seizure parameters. Serum vitamin E and lipid profile were adversely affected indicating the need for higher doses of vitamin E and longer duration of follow up.

Keywords: ketogenic diet, intractable epilepsy, vitamin E

INTRODUCTION

Epilepsy is a chronic neuronal disorder characterized by recurrent (two or more) epileptic seizures that usually recur unpredictably in the absence of provoking factors and having a high impact on the individual as well as on society as a whole. An epileptic seizure is a clinical presentation which is linked to an abnormal and excessive or hypersynchronous activity from a set of neurons in a specific locus of the brain (*Shakirullah et al., 2014*).

This might affect, for example, the muscles, the senses, consciousness, or a combination. A seizure can be focal (confined to one part) or generalized (spread widely throughout the brain and leading to loss of consciousness) (*Shakirullah et al., 2014*).

Epilepsy is one of the most common neurological disorders that affects at least 50 million people world wide (*De Boer et al., 2008*). Although the prognosis of the majority of patients is good; up to 20-30% do not respond to adequate antiepileptic drugs and said to suffer from drug resistant epilepsy (DRE) (*Geerts et al., 2010*).

Drug resistance can be defined as ‘failure of adequate trials of two tolerated, appropriately chosen and used anti-epileptic drug schedules– whether as monotherapy or in combination – to achieve sustained seizure freedom (*Kwan et al., 2010*).

Patients suffering from intractable epilepsy are at increased risk for cognitive, behavioral and psychiatric disturbance (*Ekinci et al., 2009*).

Currently, the treatment methods for drug resistant epilepsy are surgery, vagus nerve stimulation, new medications, and the Ketogenic diet. Over the last decade, the ketogenic diet has gained popularity as another treatment option for this group of patients. Dietary measures have been described for the treatment of epilepsy since ancient times (*De Kinderen et al., 2011*).

Despite the lack of a well-defined mechanism of action, numerous reports have appeared in the literature suggesting the benefit of this diet in reducing the frequency of seizures. Furthermore, the ketogenic diet side effects are generally transient, minor and can be treated without having to discontinue the diet (*Rogovik and Goldman, 2010*).

While the ketogenic diet now is recognized as an accepted treatment of children with intractable epilepsy, its use in all age groups is generally restricted to the treatment of last resort as its efficacy and safety remain controversial (*Rubenstein, 2008*).

Any calorically restricted diet may not provide all nutritional requirements and the limited number of food available on a ketogenic diet may cause deficiencies. At very