Effect of Magnesium Supplementation on Hyperactivity in Pediatric Patients with Attention Deficit Hyperactivity Disorder (ADHD)

Thesis

Submitted for partial fulfillment of master degree in Pediatrics

By Rana Abd El Hakim Ahmed

 $\mathcal{M}.\mathcal{B}.\mathcal{B}.\mathcal{C}h$

Faculty of medicine - Ain Shams University

Supervised by

Prof. Dr. Farida El Baz Mohamed El Baz

Professor of Pediatrics
Faculty of medicine - Ain Shams University

Dr. Heba Hamed El Shahawi

Assistant Professor of Psychiatry
Faculty of medicine - Ain Shams University

Dr. Sally Soliman Ahmed Zahra

Lecturer of Pediatrics Faculty of medicine - Ain Shams University

> Faculty of Medicine Ain Shams University 2011

تأثير إضافة الماغنيسيوم على فرط الحركة في الأطفال المصابين بمرض فرط الحركة و قلة الانتباه

رسالة عملية مقدمة توطئة للحصول على درجة الماجستير في طب الأطفال

مقدمة من

الطبيبة / رنا عبد الحكيم أحمد محمود

بكالوريوس الطب والجراحة العامة - جامعة عين شمس

تحت إشراف

الأستاذة الدكتورة / فريدة الباز محمد الباز

أستاذ طب الأطفال كلية الطب – جامعة عين شمس

الدكتورة / هبه حامد الشهاوي

أستاذ مساعد الطب النفسي كلية الطب – جامعة جامعة عين شمس

الدكتورة / سالى سليمان أحمد زهرة

مدرس طب الأطفال كلية الطب – جامعة جامعة عين شمس كلية الطب جامعة عين شمس

Summary

Attention deficit hyperactivity disorder (ADHD) is a common neuropsychiatric disorder (Wang et al., 2011).

Reports on the prevalence of ADHD/HKD have varied from 0.5% to 16%. It accounts for most mental health referrals of children (*Aguiar et al.*, 2010) (*Bange*, 2011).

Traits of inattention, impulsivity, and motor hyperactivity characterize children diagnosed with attention-deficit/hyperactivity disorder (ADHD), whose inhibitory control is reduced (*Adriani et al.*, 2011).

There is a high level of comorbidity with developmental and learning problems as well as with a variety of psychiatric disorders. ADHD is highly heritable, although there is no single causal risk factor and non-inherited factors also contribute to its aetiology. The genetic and environmental risk factors that have been implicated appear to be associated with a range of neurodevelopmental and neuropsychiatric outcomes, not just ADHD (*Thapar et al.*, 2011).

Attention deficit and hyperactivity disorder (ADHD) is not restricted to children. Abundant evidence from follow-up studies accumulated since the 1970s supports the concept of ADHD in adulthood. Genetic research points to a heritability of 76%, and neuroimaging studies have reported structural and functional brain abnormalities in patients with ADHD. Contrary to popular belief, ADHD is not a culturally bound disorder and has been described worldwide (*Bolea et al.*, 2011).

List of Contents

	Page
List of abbreviations	I
List of tables	VI
List of figures	IX
Introduction	1
Aim of the work	3
Chapter I: Historical review	
Chapter II: Clinical Picture, Classification Diagnosis	
and Co-Morbidities	. 11
Chapter III: Molecular Genetics Neuroscience and	
Neuropsychology	. 39
Chapter IV: Epidemiology of ADHD	. 79
Chapter V: Risk factors for ADHD	. 94
Chapter VI: Assessment of ADHD	. 94
Chapter VII: Management of ADHD	. 136
Subjects and Methods	. 161
Results	. 179
Discussion	
Summary	. 233
Conclusion	. 237
Recommendations	. 238
References	. 239
Sheet	. 317
Arabic summary	

5-HIAA 5-hydroxyindole acetic acid

American academy of child and adolescent psychiatry AACAP,

ACC Anterior cingulate cortex

ACTeRS ADHD comprehensive teacher rating scale Attention deficit disorders evaluation scale **ADDES**

Attention deficit hyperactivity disorder **ADHD**

AMP Adenosine monophosphate

Adenosine triphosphate Behavior assessment system for children **BASC**

BPD Bipolar disorders

ATP

CAM Complementary and alternative medicine

Cyclic adenosine monophosphate cAMP

Child behavior checklist **CBCL**

Conduct disorder CD

COMT Catechol-o-methytransferase **CPT** Continuous-performance test

DA Dopamine

DAT1 Dopamine transporter gene

DAT-KO Dat1 knock-out mice

Dopamine-beta-hydroxylase **DBH**

Docosa-hexaenoic acid DHA

DISC Diagnostic Interview Schedule for Children

dlPFC, vlPFC Dorsolateral or ventrolateral prefrontal cortex

DOPA Dihydroxy-phenylalanine

Dopa Dopa decarboxylaseDRC Daily Report Cards

DRD2 gene Dopamine receptor D2 gene

DZ Dizygotic

EEG Electro encephalogram

EFAs Executive Function
EFAs Essential fatty acids

EPA Eicosa-pentaenoic acid

EVT Expressive Vocabulary Test

FAS Fetal alcohol \$

FDA Food and drug administration

F MRI Functional magnetic resonance imaging

GABA Gamma amino butyric

HCN Hyperpolarization-activated cyclic nucleotide-gated

HD Hyperactive disorder

HTMA Hair tissue mineral analysis

ICD-10 International Classification of DiseasesICP-MS Inductively Coupled Mass Spectroscopy

IH Intermittent hypoxiaIQs Intelligence quotient

KABC-II Kaufman Assessment Battery for Children

KBIT Kaufman Brief Intelligence Test
KMS Kansas Marital Satisfaction Scale

KSADS- PL, Kiddie Schedule for Affective Disorders and

Schizophrenia for School Age Children-Present and

Lifetime Version

LBW low birth

LD Learning Disabilities

LMAT Locke-Wallace Marital Adjustment Scale

LPHN3 Latrophilin 3

MAO-A and

MAO-B

Monoamine oxidase A and B

MBD Minimal Brain Dysfunction

Mg Magnesium
Mn Manganese

MPR Membrane potential ratio

MSCS Multi-dimensions Self-Concept Scale

MVPT-R Motor Free Visual Perception Test Revised

MZ Monozygotic

NAcc Nucleus accumbens

NET Noradrenergic transporter

NMDA N-methyl D-aspartate

ODD Oppositional Defiant Disorder

OFC Orbitofrontal cortex

OSA Obstructive sleep apnea

PANDAS Pediatric Autoimmune Diseases Associated with

Streptococcal infections

Pb Lead

PCBS Polychlorinated Biphenyls

PDICs Pregnancy, delivery and infancy complications

PET Positron emission topography

PFC Prefrontal cortex
PKU Phenylketonuria

PNMT Phenylethanolamine N-Methyltransferase

PPVT-III The Peabody Picture Vocabulary Test-III, Third

Edition

PSI parenting stress index

PTSD Post-Traumatic Stress Disorder

QEEG Quantitative EEG

QoL Quality of life

RD Reading Disability

RDA Recommended daily allowance

redoxReduction oxidationREMRapid eye movement

ROC Curve (), Receiver Operating Characteristics

ROS Reactive oxygen species

RTH Resistance to thyroid hormones

RWD Reading writing disorder

S.C.T Sluggish Cognitive Tempo

SCL- Symptom checklist 90-revised

SCL-90-R Symptom checklist 90-revised

SDB Sleep disordered breathing

SEG Socio-economic groups

SES Socioeconomic status

SIGN Scottish Intercollegiate Guidelines Network

SPECT Single photon emission computed tomography

SSRI Selective serotonin reuptake inhibit

SUD Substance use disorder

TCAs Tricyclic antidepressants

TCPs Trichlorophenols

TH Tyrosine hydroxylase

TOLD-P Test of Language Development-Primary

TOMAL Test of Memory and Learning

TRPM6 Transient receptor potential melastatin 6

TS Tourette syndrome

US FDA United states food and drug administration

VNTR Variable number of tandem repeats

VTA Ventral tegmental area

WIAT Wechsler Individual Achievement Test
WISC Wechsler intelligence scale for children

WRAML Wide Range Assessment of Memory and Learning

Zn Zinc

List of Tables

table	Title	Page
1	Environmental risk factors for mental health disorders	94
2	Common issues in assessment of ADHD	117
3	Effective behavioral adolescents with ADHD techniques for children and adolescents with ADHD	149
4	Recommended Dietary Allowances for magnesium for children and adults	155
5	Scoring of conner scale	172
Results	S	
1	ROC Curve for the diagnosis of decreased Magnesium level in hair among hyperactive children	179
2	Comparison between cases and controls as regards personal characteristics	180
3	Comparison between cases and control as regards serum and hair Magnesium level	181
4	Correlation between Magnesium level in hair and psychiatric scales among children with ADHD	183
5	Correlation between Magnesium level in serum and psychiatric scales among children with ADHD	186
6	Comparison between cases with normal (group A) and low hair Magnesium (group B) as regards personal and medical characteristics	187
7	Comparison between cases with normal and low hair Magnesium as regards symptoms	190
8	Comparison between cases with normal (group A) and low hair Magnesium (group B) as regards different psychiatric scales	191

List of Tables

table	Title	Page
9	Comparison between Magnesium among treated (group B1) and untreated low hair Magnesium cases (group B2), as regards categories completion score at baseline and at follow up	193
10	Comparison between Magnesium treated (group B1) and untreated low hair magnesium cases (group B2), as regards improvement in categories completion at follow up	194
11	Comparison between Magnesium treated (group B1) and untreated low hair Magnesium cases (groupB 2), as regards Conceptual level score at baseline and at follow up	195
12	Comparison between Magnesium treated (groupB 1) and untreated low hair Magnesium cases(group B2), as regards improvement in Conceptual level at follow up	196
13	Comparison between Magnesium treated (group B1) and untreated low hair Magnesium cases (group B2), as regards oppositional score at baseline and at follow up	197
14	Comparison between Magnesium treated (group B1) and untreated low hair Magnesium cases (group B2), as regards improvement in oppositional level at follow up	198
15	Comparison between Magnesium treated (groupB 1) and untreated low hair Magnesium cases (group B2), as regards inattention score at baseline and at follow up	199
16	Comparison between Magnesium treated (group B1) and untreated low hair Magnesium cases (group B2), as regards improvement in inattention level at follow up	200

List of Tables

table	Title	Page
17	Comparison between Magnesium treated (group B1) and untreated low hair Magnesium cases(group B2), as regards Hyperactivity score at baseline and at follow up	201
18	Comparison between Magnesium treated (group B1) and untreated low hair Magnesium cases (group B2), as regards improvement in hyperactivity level at follow up	202
19	Comparison between magnesium treated (group B1) and untreated low hair Magnesium cases (group B2), as regards impulsivity score at baseline and at follow up	203
20	Comparison between Magnesium treated (group B1) and untreated low hair Magnesium cases(group B2), as regards improvement in impulsivity level at follow up	204
21	Comparison between psychiatric scales at baseline and at follow up among Magnesium treated cases (group B1)	206
22	Comparison between psychiatric scales at baseline and at follow up among untreated (group B2) low hair Magnesium cases	207
23	Adverse effects among magnesium treated cases (group B1)	208

List of Figures

Fig.	Title	Page
1	Overlap of ADHD and comorbid disorders	25
2	Diagram of the human brain showing the right hemisphere, and particularly the location of the caudate nucleus (striatum), globus pallidus, and cerebellar vermis	41
3	Schematic model of the dorsal and ventral neural pathways associated with 'Cool' and 'Hot' cognition	59
4	Grip Test	133
5	Some good sources of magnesium	153
6	Ginkgo is a natural supplement used by some with ADHD	159
7	Hair sampling	167
8	Coupled Mass Spectroscopy	168
9	Screenshot from a computerized version of the Wisconsin Card sort	175
Results		
1	Using ROC Curve (Receiver Operating Characteristics), the cut off value for deficient Magnesium level in hair was equal or less than 60	179
2	Comparison between cases and control as regards serum Magnesium level	182
3	Comparison between cases and control as regards hair Magnesium level	182
4	Scatter diagram for correlation between magnesium level in hair and total IQ among children with ADHD	184
5	Scatter diagram for correlation between magnesium level in hair and hyperactivity among children with ADHD	185
6	Comparison between cases with normal and cases with low hair Magnesium level as regards sex	188
7	Comparison between cases with normal and cases with low hair Magnesium level as regards socioeconomic status	189

List of Figures

Fig.	Title	Page
8	Comparison between cases with normal (group A) and	192
	low hair Magnesium (group B) as regards verbal skills	
	of the wechesler scale	
9	Improvement of psychiatric scales at follow up among	205
	treated (group B1) and untreated group (group B2).	

