Prolactin, Thyroid hormones, and Growth hormone levels in Epileptic children on Antiepileptic drugs

Thesis
Submitted for partial fulfillment
Of Master degree in Pediatrics

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M.B.B.CH, (2002)

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Cairo
2006

Acknowledgement

Thanks GOD for the strength he gave me to finish this work.

I am so much grateful to all my professors who helped me through out my college & practical life.

Special thanks to professor Dr.Hamed El-Khayat who have always been of great support, professor Dr.Hanaa Amer and last but not least Dr.Maha Awadalah who helped me with every step of this work.

My father who did his best to help me in all aspects of life and work, my friends who were always supportive and helpful.

My mum who didn't live enough to see this work done, I dedicate every minute of effort spent in this work to her and hope she will be proud of me, may GOD bless and rest her soul.

Yasmin galal

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List of Abbreviations

- ACTH Adrenocorticotropic hormone
- ADH Antidiuretic hormone
- AEDs Anti-epileptic drugs
- ALT (SGPT) Alanine transaminase
- AMPA Alpha amino 3 hydroxy 5 methylisoxazole propionic acid
- AST (SGOT) Aspartate transaminase
- AV block Atrioventricular block
- BDZ Benzodiazepines
- BECCT Benign epilepsy of childhood with centrotemporal spikes
- BMEI Benign myoclonic epilepsy of infancy
- BMI Body mass index
- BOE Benign occipital epilepsy
- BUN Blood urea nitrogen
- CAE Childhood absence epilepsy
- cAMP Cyclic adenosine monophosphate
- CBZ Carbamazepine
- CNS Central nervous syndrome
- CT Computerized tomography
- EEG Electroencephalography
- ELISA Enzyme linked immunosorbent assay
- FLAIR Fluid attenuated recovery
- FSH Follicle stimulating hormone
- GABA Gamma amino butyric acid
- GAD Glutaric acid decarboxylase
- Gamma GT Gamma glutamyl transferase
- GBP Gabapentin
- GH Growth hormone
- GHBP Growth hormone binding protein
- GHRH Growth hormone releasing hormone
- GTC Generalized tonic clonic convulsins
- hCG Human chorionic gonadotropins
- HDL High density lipoprotein
- HIV Human immunodeficiency virus
- HLA Human leukocyte antigen
- IGF-1 Insulin growth factor-1
- IGFBP3 Insulin growth factor binding protein 3
- ILAE International league against epilepsy

- IM injection Intramuscular injection
- IV injection Intravenous injection
- JAE Juvenile absence epilepsy
- JME Juvenile myoclonic epilepsy
- LDH Lactate dehydrogenase
- LGS Lannox-Gastaut syndrome
- LH Lutenizing hormone
- LTG Lamotrogine
- MHD 10 monohydroxy metabolite
- MRI Magnetic resonance imaging
- mRNA Messenger ribonucleic acid
- MRS Magnetic resonance imaging
- MSH Melanocytes stimulating hormone
- NMDA N-Methyl-D-aspartate
- OFC Occipitofrotal circumference
- OXC Oxcarbazepine
- PET Positron emission tomography
- PET-FDG Positron emission tomography-18 fluorodeoxyglucose
- PHB Phenobarbital
- PHT Phenytoin
- PRL Prolactin
- PSW Polyspike and Wave
- REM Rapid eye movement
- RNA Ribonucleic acid
- SPECT Single photon emission computed tomography
- SPGR Spoiled gradiant recall images
- SW Spike and Wave
- TBG Thyroid binding globulin
- TCAs Tricyclic antidepressants
- TLE Temporal lobe epilepsy
- TRH Thyrotropin releasing hormone
- TSH Thyroid stimulating hormone
- VGB Vigabatrin
- VPA Valproic acid

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Introduction

Patients with epilepsy may have several hormones with different serum levels than those of similarly aged healthy people ***(Macphee et al, 1988).***

Moreover, patients with epilepsy often complain about symptoms that may be caused by disturbances in their hormonal balance ***(Cramer & Jones, 1991).***

The liver enzyme-inducing properties of Antiepileptic drugs (AEDs) may account for changes in serum hormone levels by accelerating their metabolism; or AEDs may cause a decrease in free hormone levels by increasing the concentration of hormone-binding proteins ***(Stoffel et al, 1998).***

Enzyme-inducing AEDs are known to result in decreased thyroid hormones. Recent studies found reduced serum thyroid hormone concentrations in men and young girls treated with carbamazepines. However, all patients were clinically euthyroid, and these changes were reversible after AED withdrawal ***(Pack, 2005).***

Valproate medication is associated with metabolic and endocrine changes in female patients ***(Isojatvi et al, 2001).***

Carbamazepine therapy has certain effects on thyroid function: it decreases the serum thyroid hormone levels, but allows the serum thyrotropin concentration and TSH responses to thyrotropin-releasing hormone to remain normal. It has been speculated that these low serum thyroid hormone levels are due to the induction of the hepatic P450 enzyme system by carbamazepine ***(Verrotti, et al, 2001)***

Epileptic seizures have a transient effect on serum pituitary hormone and cortisol levels ***(Rao & Stefan, 1989).*** A moderate increase in serum prolactin, due to anticonvulsant medication, has been reported ***(Bauer, 1996).***

Moreover, significantly lower prolactin levels were observed in patients treated with carbamazepine, compared with untreated patients with epilepsy. Thus, AEDs may increase or decrease serum prolactin ***(Isojarvi et al, 1989).***

Aim of The Work

To study the effect of AEDs on the functions of the endocrine system in epileptic patients.

Levels of pituitary hormones as Prolactin and TSH, as well as Growth hormone will be evaluated in epileptic patients receiving AEDs compared to healthy age-matched control group.

This allows insights into the endocrine system so that we could evaluate the extent to which epilepsy & long term AEDs influence the endocrine functions of such patients.

Chapter one

Epilepsy

Definition & Historical background:

Epilepsy is a seizure disorder caused by a sudden change in electrical activity in the brain.***(Lechtenbert et al., 1999).*** Epilepsy is a disorder characterized by the occurrence of at least 2 unprovoked seizures. Seizures are the manifestation of abnormal hypersynchronous discharges of cortical neurons. The clinical signs or symptoms of seizures depend on the location and extent of the propagation of the discharging cortical neurons. ***(Rho et al., 2004)***

J.H. Jackson gave direction to the understanding of epilepsy in the late 19th century by carefully analyzing individual cases. From his observation, Jackson formulated the modern definition of epilepsy: " An occasional, excessive, and disorderly discharge of nerve tissue." Jackson further concluded, " This discharge occurs in all degrees; it occurs with all sorts of conditions of ill health at all ages, and under innumerable circumstances." His emphasis on the clinical description of a seizure, beginning with the mode of onset, led to the concept of focal epilepsy with subsequent spread of discharging cells. ***(Jackson, 1951).***

GENETICS AND EPILEPSY:

CHANNELOPATIES

Mechanism of channelopathies

Epilepsy is a disorder of altered neuronal excitability. Ion channels underlie the physiology of excitable membranes ***(Treiman et al., 2001).***

Type	Syndrome	Inheritance	chromosome	Gene	Function
Idiopathic generalized	Benign familial neonatal convulsions	Autosomal dominant (AD)	20q	KCNQ2	Voltage gate K channel
	Childhood absence epilepsy with generalized tonic-clonic seizures	Complex	8q24		
	Childhood absence evolving to juvenile myoclonic epilepsy	Complex	1p		
	Juvenile absence epilepsy	Complex	21q22.1	GRIK1	GluR5(Kainate receptor)
Situation related siezures	Febrile	AD	8q13-21		
	Generalized epilepsy plus febrile seizures	AD	2q21-33	SCN1B	Sodium channel B subunite
	Generalized epilepsy with febrile seizures plus	AD	19q13.1		

Localization related	Benign infantile familial convulsions	AD	9q11-13		
	Autosomal dominant nocturnal frontal lobe epilepsy	AD	20q13.3	CHRNA4	
	Autosomal dominant temporal lobe epilepsy	AD	10q22-24		
	Rolandic epilepsy	Complex	15q14		
Progressive	Lafora's disease	Recessive	6q24	EPM2A	Tyrosin phosphate
	Northern with mental retardation	Recessive	8pter-23	CLN8	Cathepsin B

Table (1) Genetics & Epilepsy (Treiman et al., 2001)