FASTING SERUM INSULIN AND LEPTIN LEVELS IN EPILEPTIC PATIENTS

Thesis

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Neurology and Psychiatry

By

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CONTENTS

Page

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS:

ADH	: Antidiuretic hormone
AEDs	: Antiepileptic drugs
AgRP	: Agouti-related peptide
AIDS	: Acquired immunodeficiency syndrome
APoA1	: Apolipoprotien A1
BMI	: Body mass index
CAD	: Coronary artery disease
CART	: Cocaine & amphetamine regulated transcript
CBZ	: Carbamazepine
CNS	: Central nervous system
CRP	: C–reactive protein
CYP3A4	: Cytochrome enzyme (P3A4)
EEG	: Electroencephalogram
ELISA	: Enzyme linked immunosorbant assay
FDA	: Food & Drug administration
FFAs	: Free fatty acids
GABA	: Gamma amino butyric acid
GAT1	: GABA transporter 1
GBP	: Gabapentin
GLUT4	: Glucose receptor type 4
HDA1C	: Histone deacetylase-1
HDL	: High density lipoprotein
HIV	: Human immunodeficiency virus
HLA	: Human leucocytic antigen
HOMA/IR	: Homeostasis model of insulin resistance
IL6	: Interleukin 6
ILAE	: International league against epilepsy
IRS-PI3-K	: Intrinsic receptor substrate-phosphatidyl inositol 3-kinase
JAK	: Janus kinases
LCAT	: Lecithin cholesterol acyl transferase
LDL	: Low density lipoprotein
LH	: Lateral hypothalamus
LPL	: Lipoprotein lipase
Mc4R	: Melanocortin 4- receptor
MSH	: Melanocyte stimulating hormone
NAFLD	: Non-alcoholic fatty liver disease
NPY	: Neuropeptide Y
PAI-1	: Plasminogen activator inhibitor-1

PC-1 : Prohormone convertase-1
PCOs : Polycystic ovaries
PGI2 : Prostacyclin
PoMC : Pro-opiomelanocortin
PPARr : Peroxisome proliferator activator receptor
Sd LDL : Small dense LDL
SIADH : Syndrome of inappropriate secretion of ADH
STAT : Signal transducer & activator of transcription
TG : Triglyceride
TGB : Tiagabine
TNFα : Tumor necrosis factor α
VEGF : Vascular endothelial growth facto
VMH : Ventromedial hypothalamus
VPA : Valproate

ABSTRACT

Background: Obesity being a common medical problem due to its complications such as atherosclerosis, diabetes mellitus etc., a number of studies were directed towards its causes. Among these causes is drug intake e.g. some antiepileptic drugs, oral contraceptive pills and others. Accordingly the present study is focused on weight gain observed with antiepileptic drugs and its relation to leptin and insulin hormones. **Objective**: The aim of this work is to study the role played by leptin & insulin hormones in weight gain induced by antiepileptic drugs. **Subjects & Methods:** This study was carried out on 40 epileptic patients, and 19 healthy subjects, where leptin, insulin levels and BMI were measured in both groups. **Results:** There was high statistically significant difference in insulin & leptin hormones between cases & controls as well as a statistically significant difference in leptin levels between valproate & carbamazepine subgroups being higher in valproate treated patients. **Conclusion**: The increased serum leptin levels was not associated with increased body weight in epileptic patients as assessed by BMI but was more influenced by anti-epileptic drug intake, especially valproate.

Keywords:
Obesity,
Epilepsy,
Insulin
Leptin hormones

INTRODUCTION
AND
AIM OF THE WORK

INTRODUCTION

Epilepsy is a common chronic neurological problem. Its treatment is often for years or even life long **(Hauser, 1997)**. It should be noted that patients with epilepsy may manifest metabolic adverse effects throughout the course of their management with antiepileptic drugs (AEDs), which on long-term may impair individual's overall function. So during managing patients with epilepsy, awareness about different metabolic consequences associated with epilepsy and its medications that may impair individual's overall function should be present **(Hamed and Abdellah, 2004; Hamed and Nabeshima, 2005; Hamed** *et al.,* **2005, 2006).**

Weight gain not only affects body image and self-confidence with adverse psychological effects leading to non-compliance to medications, but is also associated with pathologic consequences related to obesity as reproductive disorders, dyslipidemia, hypertension, insulin resistance, diabetes mellitus and atherosclerosis and its related vascular complications **(Kawachi, 1999).**

Marked bodyweight gain can be caused by drugs belonging to many pharmacological groups and is a common problem with the use of anticonvulsants. This has been observed with valproic acid, carbamezapine and some newer anticonvulsants as gapabentin **(Jallon and Picard, 2001)**. Topiramate **(Ben-Menachem** *et al.,* **2003),** felbamate **(Ketter** *et al.,* **1999)** and zonismaide **(Biton, 2003),** cause weight loss. While stable body weight is observed with diphenylhydantoin **(Hogan** *et al.,* **2000),** oxcarbazepine **(Glauser, 2001),** levetiracetam **(Gidal** *et al.,* **2003),** lamotrigine **(Bowden** *et al.,* **2006)** and tiagabine **(Hogan** *et al.,* **2000).**

Potential mechanisms of anticonvulsants -associated body weight gain are not yet clear and different between drugs used. The involvement of lower blood glucose level, which may stimulate eating through an effect on the hypothalamus, constitutes one of the possible mechanisms. Lowered blood glucose levels may result from competition between the drug and long chain fatty acids; an increased availability of the long chain fatty acids stimulates insulin production and lowers the serum glucose levels. Another possible explanation for lowered blood glucose level may be a deficiency in carnitine directly caused by the drug, which would result in a reduction of fatty acid metabolism and an increase in glucose consumption **(Jallon and Picard, 2001)**.

The two common homeostatic hormones, insulin, a protein product of pancreatic β-cells and leptin, a protein product of adipoctyes **(Zhang** *et al.,* **2004)** have been expected to form a common link to weight gain in epilepsy with the use of some AEDs **(Isojarvi** *et al.*, **1996)**. In general, normally, they act together to balance food intake and energy expenditure **(Elmquist** *et al.,* **1999)**. Data regarding the effect of various AEDs on insulin and leptin levels are controversial **(Pylvanen** *et al.*, **2002).**

AIM OF THE WORK

1. The aim of this study is to find the role played by leptin and insulin hormones in weight gain induced by some antiepileptic drugs.
2. To detect the effect of obesity on seizure frequency.