Evaluation of Serum Neurotensin Level in Fatty Diet Induced Obesity

Thesis

Submitted for Partial Fulfillment of Master Degree in Physical Medicine, Rheumatology and Rehabilitation

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2019

قياس مستوى النيوروتنسين فى المصل فى حالات تناول الطعام الدهنى المسبب للسمنة

رسالة

توطئة للحصول علي درجة الماجستير فى الطب الطبيعى والروماتيزم والتأهيل

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٢٠١٩

سورة البقرة الآية: ٣٢

Acknowledgement

First and foremost, thanks to **ALLAH** *almighty for knowledge and understanding that He grants me.*

Can never serve me to express my deepest gratitude to all my professors who never retained any effort to guide me through my path morally and scientifically.

I am sincerely indebted to ***Prof. Dr. Mohamed Ragaai El-Helow*** *Professor of Physical Medicine, Rheumatology and Rehabilitation, for his guidance and sincere help from beginning of the current work. Without his care this work could never be accomplished.*

I am deeply grateful for ***Prof. Dr. Iman Mahmoud Ghanima****, Professor of Physical Medicine, Rheumatology and Rehabilitation, for her valuable help and guidance. I am deeply indebted to her guidance, sincere directions and close supervision.*

I would like to express my deepest thanks and sincere gratitude to ***Dr. Dalia Mohamed Ezz El Din Mahmoud*** *Assistant Professor in Physical Medicine, Rheumatology and Rehabilitation, for giving me the privilege of working under her supervision, for her encouragement, her patience and valuable instructions.*

I would like to express my deepest thanks and sincere gratitude to ***Dr. Dalia Samaha*** *Assistant professor in clinical pathology department for her patience and valuable instructions.*

Jehan Magdy Mahmoud Moharram*.*

Dedication

This work is dedicated to …

My beloved Parents, to whom I owe everything I ever did in my life and will achieve.

My husband My brother and my dear friends for their support.

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List of Abbreviations

ACC	:	Acetyl-coa carboxylase
AgRP	:	Agouti-related peptide
AMPK	:	Adenosine monophosphate kinase
AP	:	Area postrema
APPL1	:	Adaptor protein, phosphotyrosine interaction, ph domain, and leucine zipper-containing protein 1.
ARC	:	The arcuate nucleus
BDNF	:	Brain-derived neurotrophic factor
BMI	:	Body mass index
CART	:	Cocaine- and amphetamine-regulated transcript.
Cck	:	Cholecystokinin
CRH	:	Corticotrophin-releasing hormone
CRP	:	*C-reactive protein*
CVD	:	Cardiovascular disease
DM	:	Diabetes mellitus
DMH	:	Dorsomedial nucleus
DNA	:	Deoxyribonucleic acid
FAS	:	Fatty acid synthase
FDA	:	Food and drug administration
FTO gene	:	Fat mass and obesity associated gene
GAL	:	Galanin
GLP	:	Glucagon-like peptide
GLP-1	:	Glucagon like peptide-1
HDL-C	:	High density lipoprotein cholesterol
H.S	:	Highly significant
HNF-4	:	Hepatocyte nuclear factor
ICAM	:	Intercellular adhesion molecule
IL-12	:	Interleukin- 12
IL-6	:	Interleukin- 6
IR	:	Insulin receptor
IRS	:	Insulin-receptor substrate
LDL-C	:	Low density lipoprotein cholesterol
LH	:	Lateral nuclei
LHA	:	Lateral hypothalamic area
LPL	:	Lipoprotein lipase

MAOIs	:	Monoamine oxidase inhibitors
MC4R	:	Melanocortin 4 receptors
MCH	:	Melanin-concentrating hormone
MIP-1α	:	Macrophage inflammatory protein 1-alpha
MSH	:	Melanocyte-stimulating hormone
MUFAs	:	Mono unsaturated fatty acids
NAFLD	:	Non-alcoholic fatty liver disease
NF-κB	:	Nuclear factor-kappab
NPY	:	Neuropeptide y
N.S	:	Non significant
NT	:	Neurotensin
NTR	:	Neurotensin receptor
NTS	:	Nucleus of the solitary tract
PCOS	:	Polycystic ovary syndrome
PFA	:	Perifornical area
POMC	:	Pro-opiomelanocortin.
PPAR-α	:	Peroxisome proliferator-activated receptor alpha.
PPARγ	:	Peroxisome proliferator-activated receptors gamma.
PUFAs	:	Polyunsaturated fatty acids
PVN	:	Paraventricular nucleus
PYY	:	Peptide y
SFAs	:	Saturated fatty acids
SORL	:	Sortilin-related receptor
SQ-FFQ	:	Semi-quantitative food frequency questionnaire
sTNFR1	:	Soluble tumour necrosis factor receptors
T2DM	:	Type 2 diabetes mellitus.
TC	:	Total cholesterol
TG	:	Triglycerides
TNF-α	:	Tumor necrosis factor α
TRH	:	Thyrotropin-releasing hormone
VMH	:	Ventromedial nucleus
WHO	:	World health organization

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Abstract

Introduction: Neurotensin is expressed in the brain as well as it is localized in specialized enteroendocrine cells of the small intestine.

Objectives: This paper aims to evaluate the serum level of neurotensin in various grades of obesity and it's relation to fatty diet.

Patients and methods: A sample of 60 patients were subjected to Full medical History, bowel habits , detailed dietary habits (Detailed fat-intake questionnaire) and body mass index (BMI). Also serum neurotensin , random blood sugar, thyroid profile and lipid profile were measured. Patients were subdivided into four groups according to their degree of obesity as follow: fifteen overweight patients, fifteen obese class I patients, fifteen obese class II patients and fifteen obese class III patients. Twenty five apparently healthy non obese individuals of matched age and sex were taken as a control group.

Results: Our study revealed 84% rise of the mean NT in cases compared to controls with highly statistical significant difference. Significant positive correlation was found between serum neurotensin, high cholesterol, low HDL and total fat intake questionnaire. But no correlation was found between serum neurotensin and TGs, LDL, age and sex.

Conclusion: Our limited data suggest that serum neurotensin may play a potentially important role in the development of obesity in people with high BMI consuming fatty diet.

Key words: neurotensin, obesity, fatty diet.

INTRODUCTION

Obesity and its associated comorbidities as diabetes mellitus and hepatic steatosis contribute to approximately 2.5 million deaths annually and are among the most prevalent and challenging conditions confronting the medical profession ***(Guh et al., 2009).***

Obesity increases the likelihood of various diseases and conditions, particularly cardiovascular diseases, type 2 diabetes, obstructive sleep apnea, certain types of cancer, osteoarthritis and depression **(*Luppino et al., 2010).***

Major recent advances in our understanding of the basic neurobiology of appetite and energy homeostasis have identified numerous targets for potential anti-obesity drug development ***(Bray et al., 2016).***

Neurotensin (NT) attenuates the activation of Adenosine monophosphate (AMP-activated protein kinase AMPK) and stimulates fatty acid absorption in mice and in cultured intestinal cells, and this occurs through a mechanism involving neurotensin receptor 1 (NTR1) and neurotensin receptor 3 (NTR3) (also known as sortilin). Consistent with the findings in mice, expression of NT in *Drosophila* midgut enteroendocrine cells results in increased lipid accumulation in the midgut, body fat , and oenocytes (specialized hepatocyte-like cells) and decreased AMPK activation ***(Melander et al., 2012).***

Recent work reporting that NT-deficient mice are protected against diet-induced obesity. Interestingly, the beneficial metabolic effects observed did not depend on effects on feeding behavior or energy expenditure but resulted from decreased intestinal fat absorption. Analogously, a selective NT receptor (NTR) antagonist decreased intestinal lipid absorption in wild-type mice ***(LI et al., 2016).***

Li et al., found that obese and insulin-resistant subjects have elevated plasma concentrations of pro-NT (a stable NT precursor fragment produced in equimolar amounts relative to NT).In longitudinal studies among non-obese subjects, high levels of pro-NT denote a doubling of the risk of developing obesity later in life. The findings directly link NT with increased fat absorption and obesity and suggest that NT may provide a prognostic marker of future obesity and a potential target for prevention and treatment ***(Li et al., 2016)***.

AIM OF THE WORK

This study is designed to evaluate the serum level of neurotensin in various grades of obesity and it's relation to fatty diet.