Evaluation Of The Role Of Gherlin Hormone In Non Alcoholic Fatty Liver Disease

Thesis

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List of Abbreviations

NAFLD:	Non alcoholic fatty liver disease
NASH:	Non alcoholic steatohepatitis
GH :.....	Gherlin hormone
DAG:	Deacyl gherlin
GHSR:	*Ghrelin/Growth Hormone Secretagogue Receptor*
GOAT:	*Ghrelin O-Acyltransferase*
ALT :.....	Alanine transaminase
AST:	Aspartate aminotransferase
ALP:	Alkaline phosphatase
GGT:.....	Gamma- glutamylgtranferase
BMI:.....	Body mass index
WC:.....	Waist circumfurance
TSH:	Thyroid stimulating hormone
FLI:	Fatty liver index

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Abstract

Background: Ghrelin, the "hunger hormone", is a peptide produced by gherlin cells in the gastrointestinal tract which functions as a neuropeptide in the central nervous system. Beyond regulating hunger, gherlin also plays a significant role in regulating the distribution and rate of use of energy. **Aim of the work:** To evaluate the level of gherlin hormone in Egyptian patients with NAFLD and its relation to severity of liver affection in such patients. **Patients and methods:** This study included 60 patients of them: 40 patients with NAFLD (Group I) subdivided into: Group l a) 20 patients with steatosis. Group l b) 20 patients with NASH; and 20 patients without NAFLD (Group II) as controls. **Results: Conclusion:** NAFLD is becoming a serious threat to public health worldwide. However, the underlying mechanisms leading to the development of NAFLD are not fully understood. The involvement of the ghrelin-GOAT system in NAFLD and a better understanding of its biology have led to the identification of pharmacologic targets and the development of pharmacologic compounds for the treatment of NAFLD and related diseases. Thus, the ghrelin-GOAT system represents a promising target for the treatment of NAFLD. **Recommendation:** The role of gherlin hormone in appetite regulation and energy metabolism is well –established and it is now recognized as a critical therapeutic agent against NAFLD.

Key words: Gherlin hormone, non-alcoholic fatty liver, liver affection

Introduction

Non-alcoholic fatty liver disease development is becoming an increasingly important disease condition, as NAFLD espesially non –alcoholic steatohepatitis (NASH) are the most common chronic liver disease in the western world, which may result in end-stage liver disease and hepatocellular carcinoma ***(Mahady, George, et al., 2014).***

The development of NAFLD is linked to food intake, as diet seems to be an important contributer to the pathogenesis of NAFLD. In a recent review, they specifically mentioned that saturated fat and fructose seem to stimulate hepatic lipid accumulation and progression into NASH, Whereas unsaturated fat, choline, antioxidants, and high proteinherea diets rich in isoflavones seem to have a more preventive effect, Therefore, it is not surprising that gut hormones that are known to control the uptake of nutrients by organs are now increasingly investigated in the light of NAFLD. ***(de Wit, et al. 2012).***

Morever, an increasing number of liver transplantations is performed due to NASH and transplantation in this cohort seems to be associated with high mortality and postoperative complications, most likely due to associated obesity and diabetes ***(Heuer, Kaiser, et al., 2012).***

The pathogenesis of NAFLD/NASH is complex but increased visceral adiposity plus insulin resistance with increased free fatty acids release play an initial key role for the onset and perpetuation of liver steatosis **(*Delhanty، Sun, et al., 2010).***

Gherlin, the "hunger hormone", is a peptide produced by gherlin cells in the gastrointestinal tract which functions as a neuropeptide in the central nervous system. Beyond regulating hunger, gherlin also plays a significant role in regulating the distribution and rate of use of energy. ***(Burger, Berner et al., 2014).***

When the stomach is empty, gherlin is secreted. When the stomach is stretched, secretion stops. It acts on hypothalamic brain cells both to increase hunger, and to increase gastric acid secretion and gastrointestinal motility to prepare the body for food intake.

The GHRL gene produces mRNA which has four exons. Five products arise: the first is the 117-amino acid preproghrelin. (It is homologous to promotilin; both are members of the motilin family). It is cleaved to produce proghrelin which is cleaved to produce a 28-amino acid gherlin (unacylated) and C gherlin (acylated). Obestatinispresumed to be cleaved from C-ghrelin ***(Seim, et al., 2010).***

Both gherlin and des-acyl gherlin (DAG) appear to have many functions and effects that are much wider than

the direct control over food intake In a recent publication, they report on the relation of the three gherlin gene products (ghrelin, DAG, and obestatin) and their involvement in those metabolic and inflammatory pathways that are linked with the development of NAFLD. ***(Delhanty, Neggers, et al., 2012).***

Ghrelin and obestatin concentrations positively correlated with fibrosis stage. Apparently, products of the gherlin gene may be important for the pathogenesis of NASH and fibrosis**.** ***(Estep, Abawi, et al., 2011).***

Ghrelin exerts its actions via the gherlin receptor GHSR-1a while DAG seems to use its own, yet unidentified receptor. Still, DAG can change gene expression receptor tissue, as DAG rapidly modulates lipogenic and *insulin* signaling pathway gene expression in metabolically active tissues ***(Delhanty, Sun, et al., 2010)***.