Study of Ghrelin Changes in Patients Exposed to Gastric Bariatric Operation

Thesis

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Presented By

Rehab Mohamed Zaher
(M.B., B.Ch.)

Supervised By

Prof. Dr. Salah Shelbaya
Professor of Endocrinology
Faculty of Medicine - Ain Shams University.

Prof. Dr. Alaa Abbas
Professor of Surgery
Faculty of Medicine - Ain Shams University.

Dr. Khaled Makboul
Lecturer of Endocrinology
Faculty of Medicine - Ain Shams University.

Faculty of Medicine
Ain Shams University

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Introduction

Small synthetic molecules called growth hormone secretagogues (GHSs) stimulate the release of GH from the pitutary gland. They act through the GHS-R, a G-Protein-coupled receptors whose ligand has only been discovered recently. Ghrelin is an endogenous ligand for GHS-R which has purified from rat stomach ***(Kojima et al., 2005)***.

Ghrelin is a gastric peptide hormone that has an important role in appetite control and GH release ***(Patterson et al., 2005)***.

It is a brain gut peptide with potent GH releasing activities, it has been suggested that the majority of circulating ghrelin originates from the stomach, with a smaller portion from the small intestine ***(Popovic et al., 2005)***.

Circulating ghrelin levels are inversely correlated with body mass index and post prandially suppressed ***(Patterson et al., 2005)***.

More over ghrelin levels differed significantly among different GIT diseases being lowest in chronic gastritis followed by gastric ulcer and highest in the acute gastritis ***(Isomoto et al., 2005)***.

Ghrelin, the novel acylated peptide acts at a central level to stimulate GH and to regulate food intake "orexigenic" ***(Caminos et al., 2005)***

Obesity is quickly becoming the most common and debilitating disorders of the developed world. In simple energy

intake, feeding must equal energy expenditure (physical activity, basal metabolism and adaptive thermogenesis) for body weight homeostasis. To maintain homeostasis, neurocircuitry must sense both immediate nutritional status and the amount of energy stored in adipose tissue, and must be able to provide appropriate output to balance energy intake and energy expenditure. The brain receives various signals that carry informations about nutritional and metabolic status including neuropeptide PYY, ghrelin, cholecystokinin, leptin, glucose and insulin. Circulating satiety signals access the brain either by leakage across circumventricular organs or by transport across the blood brain barrier. Signals can also activate sensory vagal terminals that innervate the whole GIT ***(Jobst et al., 2004).***

Ghrelin stimulates GH release and causes weight gain through increased food intake and reduced fat utilization. Ghrelin levels were shown to rise in the pre-prandial period and decrease shortly after meal consumption, suggesting a role as a possible meal initiator ***(Natalucci et al., 2005)***.

In morbidly obese individuals, ghrelin levels are low compared to lean persons. During dieting, plasma ghrelin levels increase, leading to an orexigenic signal, which could explain the lack of success of dieting in morbidly obese individuals ***(Nijhuis, 2004).***

Bariatric surgery is the only effective long-term treatment for morbid obesity ***(Perez et al., 2005).***

The increasing prevalence and associated sociodemographic disparities of morbid obesity are serious public health concerns.

Bariatric surgical procedures provide greater and more durable weight reduction than behavioral and pharmacological interventions for morbid obesity ***(Santry et al., 2005)***.

Gastric bypass has been reported to be associated with markedly suppressed plasma ghrelin levels suggesting that it is one of the possible weight reducing factors related to this procedure ***(Leonetti et al., 2003).***

The important weight loss due to bariatric surgery allows to improve and even correct, a great part of co morbidities induced by obesity, as well as quality of life, and to reduce the coming of cardiovascular and metabolic diseases in operated patients. The impact of surgical treatment on the health of the patient and quality of life also allows to reduce direct and indirect costs of morbid obesity ***(Suter et al., 2005).***

Aim of the Work:

The aim of the study is to evaluate the fasting plasma ghrelin level before and after bariatric surgery "Roux-en-y gastric bypass and adjustable silicone gastric banding" in the same patients.

Obesity

Definition of obesity:

Obesity is originally derived from the Latin word (obesus) i.e. to over eat. The modern purist's definition is "a disease of excess body fat ***(Kral, 2001)***.

The world health organization recognizes obesity as the greatest health threat of the twenty-first century ***(Campbell & Haslam, 2005)***, and obesity is considered a significant public health challenge as well as an enormous burden ***(Brunicardi et al., 2001)***. For decades, conventional wisdom has considered obesity as a disease of bad habits and weak willpower ***(Greenway, 1998)***.

Obesity is a complex disorder of appetite regulation and energy metabolism controlled by specific biological factors. In the past 10 years, great progress has been made in the scientific understanding of the pathophysiology of obesity and the interactions between genetic predisposition to weight gain and the environment ***(Labib, 2003).***

Finally, obesity is a condition in which excess body fat may put a person at health risk ***(WHO, 1998).***

Severity is based on the degree of excess body fat, which is commonly assessed using body mass index (BMI=weight (kg)/height (m^2)), which correlates body weight with height. Patients are classified as overweight, obese, or severely obese (sometimes referred to as morbidly obese). Obesity also defined as

body weight that exceeds ideal weight by20%with ideal body weight determined by population studies. Morbidly obese individuals are generally100% over ideal body weight. In 1991, the National Institutes of Health (NIH) defined morbid obesity as BMI of 35 kg/m² or greater with severe obesity-related comorbidity, or a BMI of 40 kg/m² or greater without comorbidity. Superobesity is a term sometimes used to define individuals who have a body weight exceeding ideal body weight by 225% or more, or BMI of 50kg/m² or greater ***(Schauer et al., 2003).***

Table (1): WHO classification and popular description of obesity, measured as BMI, for adult men and women:

BMI	WHO classification	Popular description
<18.5	Underweight	Thin
18.5-24	Normal	Healthy
25-29.9	Overweight	Overweight
30-34.9	Obese class I	Obese
35-39.9	Obese class II	Severe obesity
40 or more	Obese class III	Morbid obesity

(Dixon et al., 2005)

Obesity can be defined as a disease in which excess fat accumulated, such that health may be adversely affected and mortality increased ***(Kopelman, 2000)***. This definition is important for two reasons: number one it unequivocally

characterizes the condition as a disease. Number two, it associates the disease with body fat not body weight or size ***(Klein, 2001).***

Historical development of obesity:

The concept that obesity is a risk to health was clearly identified in the works of Hippocrates and frequently over the ensuing centuries. Obesity was originally discussed as part of more general texts. Scholarly theses on this subject began to appear in the late 16th century with the first monographs published in the 18th century. The value of dietary restriction, increasing exercise and reducing the amount of sleep were identified early in medical history dating at least from the time of Hippocrates. These concepts were often framed in a manner which implied a 'moral' weakness on the part of the overweight individual. The most spectacular dietary success was published by a layman in 1863 and was the forerunner to many subsequent diet books. Cases of massive obesity were identified in Stone Age carvings and have been described frequently since the time of Galen and the Roman Empire. More specific types of obesity began to be identified in the 19th century. Following the identification of the cell as the basic building block of animals and plants, fat cells were described and the possibility that obesity was due to too many fat cells was suggested. After the introduction of the calorimeter by Lavoisier, the suggestion that obesity might represent a metabolic derangement has been suggested and tested. Standards for measuring body weight appeared in the 19th century. The possibility that familial factors might also be

involved was clearly identified in the 18th and 19th century. In conclusion, most of the concepts which are currently the basis for research in the field of obesity had their origin in the 19th century and often earlier ***(Bray, 1990).***

Epidemiology:

The prevalence which is defined as total number of people in a population that are known to be overweight or obese at a given point in time. Usually expressed as a percent of the total population. The epidemic of obesity is probably a result of increasingly sedentary lifestyle combined with easy availability of palatable, high fat foods ***(Mexico, 1993)***.

Prevalence of obesity:

Obesity is the most common chronic disease in western countries affecting one third of the population ***(Melissas et al, 2002)***. According to NAASO (North American Association for the study of obesity) the prevalence of obesity in Egypt is 36% in females and 17% in males (BMI>30) ***(NAASO, Newsletter 2001).*** The prevalence of overweight and obesity have increased dramatically during the last few decades in the whole world ***(Giusti et al, 2003)***.

The National Health and Nutrition Examination Survey (NHANES) III reported that between the years 1988-1994, 2.9%of adults were extremely obese (BMI>40 kg/m^2). NHANES 1999-2000 revealed that the extremely obese population load increased by 1.8%to 4.7 % ***(Fray & Picher 2003)***.

Finally, it is worth noting that data from the Behavioral Risk Factor Surveillance System (BRFSS), which is a cross sectional telephone survey of non-institutionalized adults, conducted between the years 1986 to 2000, indicated that the prevalence of a BMI of 40 or greater quadrupled and the prevalence of a BMI of 50 or greater increased five fold in adults ***(Mokdad et al., 2001)***.

Correlation to race: Overweight for this population of 2 to 19 year-olds was defined as at, or above, the 95th percentile of the sex-specific BMI for age growth charts. The prevalence of overweight was 15–16% amongst 6 to 19 year-olds in 1999–2000, which represented a marked increase compared to similar measurements made in 1988–1994 (10.5–11.3%). Amongst the youngest group (2 to 5 years old) the overweight prevalence increased from 7.2% to 10.4% over the decade. These trends were exaggerated in non-Hispanic black and Mexican American adolescents (increase in prevalence of more than 10 percentage points between 1988–1994 and 1999–2000), so that more than 23% of adolescents of these ethnic groups were overweight in 1999–2000. Comparing data from 1999–2000 to 2001–2002 showed no indication that the prevalence of obesity amongst adults and overweight amongst children is decreasing ***(Rubenstein, 2005).***

Correlation to age: According to age, in the past two decades, the number of obese adults has doubled and obese children and adolescents, aged 6 to 18 years, have tripled ***(Dennison et al, 2002).*** For men and women the prevalence of over weight increases with each 10 year increment of age until 50 to 59 years