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Variation in blood levels of hormones in obese patients following weight reduction induced by endoscopic and surgical bariatric therapies

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ABSTRACT

Background: Beneficial clinical effects of weight reduction following bariatric therapies is not fully understood and maybe related to the complex interactions between leptin, adiponectin, visfatin, omentin, and ghrelin. The aim of study was to investigate their timeline changes associated with weight reduction and their profile in relation to the type of treatment and its efficacy.
Methods: Circulating hormones levels were analyzed before and after endoscopic and surgical procedures in 67 obese patients and compared to non-obese healthy controls.
Results: Obese patients had higher leptin levels and lower levels of adiponectin, visfatin, omentin, and ghrelin than non-obese controls. During the consecutive follow-up visits after treatment, there was a gradual decrease in leptin levels and an increase in adiponectin levels to the levels observed in non-obese. At 50–54 weeks, the ghrelin levels were lower and the levels of adiponectin and visfatin, but not omentin, were higher compared to their baseline values. BMI correlated with ghrelin and leptin levels. The percentage of total weight loss correlated positively with adiponectin levels and negatively with leptin levels. Patients with adequate weight loss had a significantly lower leptin concentration than those with treatment failure. There were timeline variations in hormone levels between endoscopic and bariatric therapies, however there were no significant differences in the median their concentration at 50–54 weeks after therapy.
Conclusion: Our study supports observations that weight loss itself, rather than the procedure type, is responsible for hormonal variation. The leptin levels reflect the best the body weight changes after bariatric therapies.

1. Introduction

Obesity is among the fastest growing diseases worldwide that increases the risk of the numbers of complications including cardiovascular diseases, diabetes mellitus and cancers. The mechanism how obesity contributes to complications is more complex and includes gastrointestinal hormones, adipokines, insulin and insulin-like growth factor signaling pathways, inflammation, immune responses, gut-brain axis, hypothalamic nervous system, and gut microbiota. Dysregulation in these systems associated with fat accumulation may lead to chronic inflammation and then to cancer development [1,2]. Among adipokines expressed by white adipose tissue, adiponectin has a protective role as it regulates insulin sensitivity, has anti-inflammatory, and anti-atherogenic properties [3,4]. Leptin regulates energy hemostasis by controlling satiety and body weight, plays a role in angiogenesis and it is a key proinflammatory factor modulating the immune system [5,6]. Recent data suggests that novel adipokines, such as omentin and visfatin, are linked to obesity and its complications regulating inflammation and insulin resistance [6,7]. In addition, ghrelin, which is the main regulator of appetite, is secreted from the stomach during the fasting period and acts on the neurons of the hypothalamus [1,8].

Abbreviations: BIB, bioenterics intragastric balloon; LAGBl, aparoscopic adjustable gastric banding; LSG, laparoscopic sleeve gastrectomy; %IBW, the percentage of initial body weight; %EWL, the percentage of excess weight loss; %TWL, the percentage of total weight loss.

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The correction of obesity-associated metabolic and inflammatory alteration is mandatory and can be achieved with weight reduction. Currently, bariatric therapies are more effective in inducing weight reduction and improving comorbidities then conservative approaches. Despite studies showing that bariatric therapies decrease body weight, improve insulin resistance and glucose metabolism, and may reduce inflammation, the exact mechanism is not well understood [1,9–12]. Several reports have described different plasma hormonal changes after bariatric surgery, but the data on the effect on the omentin and visfatin levels are sparse and conflicting [9–17]. Moreover, only a few studies have described hormonal changes, mainly ghrelin and leptin, after endoscopic placement of a balloon into the stomach (bioenterics intragastric balloon, BIB), which is a commonly used procedure, also as bridge therapy to surgery, due to its minimal invasiveness and good tolerability [18,19]. We recently found that in morbidly obese patients, weight reduction induced by BIB was connected with a decrease of leptin plasma levels and transient elevation of ghrelin levels, while the levels of these hormones remained relatively stable in obese patients treated with a low-calorie diet and physical effort [18]. There is no data on the effect of BIB therapy on plasma levels of omentin and visfatin.

Knowledge about the timeline hormonal changes with weight loss will improve the understanding of the pathophysiological mechanism of obesity. The observed changes of adipokines and gastrointestinal hormones may determine the treatment efficacy of obesity and its complications and will improve patients' selection to bariatric procedures. Therefore, the aim of the study was to assess: (i) the profile of ghrelin, leptin, adiponectin, visfatin, and omentin in obese patients; (ii) the timeline changes associated with weight reduction after endoscopic and surgical bariatric therapies; and (iii) their level changes in relation to the type of treatment and its efficacy.

2. Material and methods

2.1. Patients

This was a prospective, observational study in which we recruited obese patients qualified to the endoscopic or surgical treatment of obesity in the Department of Gastroenterology and Internal Medicine, and the Department of General Surgery and Endocrinology, Medical University of Bialystok, Poland. The study protocol was approved by the local ethics committee and conducted with the guidelines of the 1975 Declaration of Helsinki.

The inclusion criteria were: (i) BMI $\geqslant$ 40 kg/m^2 or BMI $\geqslant$ 35 kg/m^2 with at least one obesity concomitant disease (e.g. hypertension, diabetes mellitus, osteoarthritis, obstructive sleep apnea syndrome); (ii) a history of failed weight loss upon conservative treatment prior to the study; (iii) age $\geqslant$18 years; and (iv) written informed consent.

The exclusion criteria were: (i) contraindications to surgical procedure or anesthesia; (ii) severe cardiac or chronic renal disease; (iii) malignancies; (iv) active or chronic infections; (v) coagulopathy; (vi) secondary causes of obesity (e.g.: genetic syndromes, thyroid disorders, polycystic ovary syndrome, Cushing disease, hypogonadism); (vii) gastrointestinal tract diseases (e.g.: previous surgical procedures, gallstones, chronic pancreatitis, ulcer disease); (viii) hernia hiatus oesophagi >3 cm; (ix) esophagitis grade C and D according to the endoscopic Los Angeles classification; (x) untreated depression or other neuropsychiatric disorders (e.g. bulimia nervosa, schizophrenia, personality disorders); (xi) alcohol intake 6 months before the inclusion and/or during the study period; (xii) drug addiction; (xiii) use of the following drugs: antipsychotic, antidepressants, and anticonvulsants; and (xiv) lack of collaboration with the patient.

The control group consisted of sex- and age-matched healthy non-obese (BMI 18.5–24.9 kg/m^2) volunteers.

2.2. Study protocol

Ambulatory-recruited obese patients (n = 80) were then hospitalized in the Department of Gastroenterology and Internal Medicine, Medical University of Bialystok. After baseline evaluation (clinical and physical examination, laboratory tests, and upper gastrointestinal endoscopy) all patients were assessed by a team of specialists (internist, gastroenterologist, bariatric surgeon, anesthesiologist, dietician and endocrinologist if necessary).

Next, all patients underwent endoscopic or surgical treatment (the type of performed procedure was in accordance with patients preferences) and were followed up at least one year. The following control visits were performed: at 8–12 weeks, 24–28 weeks, and 50–54 weeks (Supplementary Fig. 1). The control visits included clinical, physical, and anthropometric examination, blood tests and (if necessary) consultations with a dietician and psychologist. The following anthropometric measurements were collected: weight in kg and BMI (kg/m^2). For the expression of weight loss after treatment the percentage of initial body weight (%IBW) and the percentage of total weight loss (%TWL) were used. Additionally, the percentage of excess weight loss (%EWL) after 50–54 weeks was calculated to assess adequate weight loss. The threshold of a minimum 50% EWL for surgically treated patients and a threshold of 25% EWL for endoscopic therapy were used a mark between success and failure of weight loss [20–24].

2.3. Obesity treatment

The endoscopic treatment of obesity (bioenterics intragastric balloon, BIB, Orbera, Allergan, Irvine, CA) was performed in the Department of Gastroenterology and Internal Medicine, Medical University of Bialystok. The BIB was endoscopically placed in the stomach under conscious sedation and filled with a volume of 500–550 saline with methylene blue. The device was successfully removed in all patients after 6 months. The surgical treatment of obesity was successfully performed in the Department of General Surgery and Endocrinology, Medical University of Bialystok, and consisted of either laparoscopic adjustable gastric banding (LAGB) or laparoscopic sleeve gastrectomy (LSG).

2.4. Biochemical parameters

Blood samples from the peripheral vein for the measurement of hormones were collected from patients before and after treatment during consecutive control visits. After centrifugation, plasma and serum were stored at −80 °C before analysis. The peripheral blood samples from volunteers were used as controls.

The measurements of leptin (Human Leptin Elisa, Biovendor), ghrelin (Human Ghrelin Total, RIA, Millipore), omentin-1 (Human Omentin-1 Elisa, Biovendor), visfatin (Visfatin, Elisa, Uscn Life Science Inc.), and adiponectin (Human Adiponectin, RIA, Millipore) were performed according to the manufacturer's instructions.

2.5. Statistical analysis

The STATISTICA 10.0 package was used for all analyses. Patients' characteristics were described using the relative (%) frequency. Results were described as mean and SD for the quantitative variables with parametric distribution and as median and IQR for variables with non-parametric distribution. Comparisons of quantitative variables between patients and controls were performed using the Student's t test or the Mann–Whitney U-test. For comparison of dependent variables between the consecutive