

Impact of Weight Loss Achieved Through Gastric Sleeve Surgery with Circulating Level of Ghrelin Hormone in Obese Subjects

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ABSTRACT:

BACK GROUND:

The epidemic of obesity is a major health problem in the developed world with a great influence on morbidity and mortality.

OBJECTIVE:

To evaluate serum ghrelin levels achieved through LSG and on insulin resistance and the serial changes of insulin concentration in obese patients following gastric sleeve.

SUBJECTS AND METHODS:

Twenty four patients underwent LSG with 25 controls were selected. Body mass index (BMI), waist circumference (WC), lipid profile, fasting blood sugar (FBS), glycated hemoglobin (HbA1c), fasting insulin, QUICKI and ghrelin hormone concentrations were measured for controls and patients prior LSG, then one month and three months post-surgery.

RESULTS:

A significant decline was noticed in BMI, WC, TC, TG, LDL-cholesterol, fasting insulin, and ghrelin, with significant increase in QUICKI in patients undergone LSG with significant differences in all studied parameters between patients and controls. A negative correlation was noticed between ghrelin and BMI in patients before sleeve gastrectomy.

CONCLUSION:

Ghrelin is a hormone closely linked with obesity taking into account the marked loss in appetite in the period after laparoscopic sleeve gastrectomy.

KEY WORD: obesity, bariatric surgery, ghrelin.

INTRODUCTION:

The epidemic of obesity is a major health problem in the developed world with a great influence on morbidity and mortality⁽¹⁾. Dietary and behavioral approaches to obesity have met with limited success and bariatric surgery is currently the only effective therapy for morbid obesity. Benefits of surgery include durable weight loss, improved cardiovascular profile, remission of type II diabetes, and better quality of life.⁽²⁾

Experimental data have indicated the presence of several peptides with their receptors in the hypothalamus and other parts of the central nervous system that may affect the quantity and quality of food intake.⁽³⁾ These peptides act as

sensors that transfer signals from the periphery and stimulate or inhibit appetite and food intake accordingly in order to maintain energy homeostasis; not only they regulate the amount of each meal but also long-term energy reserves (i.e. the amount of fat tissue).⁽⁴⁾ Sleeve gastrectomy usually associated with increasing satiety with a subsequent reduction of food intake due to either an elevated intragastric pressure or possibly from a decrease in ghrelin levels, which are secreted mainly by the fundus⁽⁵⁾. The delay in gastric emptying is believed to occur due to the decrease in food intake after a restrictive surgery, such as LSG.⁽⁶⁾ LSG was initially proposed as a first-stage procedure to perform in higher risk patients to achieve a significant weight loss prior to complete more complex bariatric procedures in a second stage.⁽⁷⁾

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Ghrelin is the first identified peripheral orexigenic hormone. It is produced by cells scattered throughout the gastrointestinal tract but mainly by the oxyntic cells of the stomach. Ghrelin has been proposed to have a role in meal initiation as the levels rise preprandially and fall in response to calorie ingestion.⁽⁸⁾

Circulating ghrelin levels are decreased in human obesity, and increased after diet induced weight loss, whereas weight loss after gastric sleeve was associated with markedly suppressed ghrelin levels.⁽⁹⁾ Gastric resection and removal of ghrelin secreting tissue is the major difference between laparoscopic sleeve gastrectomy and other restrictive procedures that do not lower ghrelin levels.⁽¹⁰⁾

SUBJECTS AND METHODS:

This study was conducted during the period from December 2012 until the end of June 2013. Twenty four (24) patients only (eleven males and thirteen females) followed the schedule of this prospective study who subjected to three successive examinations and blood sampling. The first examination was pre-operatively followed by two other examinations and blood sampling one month and then three months post-surgical operation. In addition twenty five (25) healthy subjects with normal body mass index (ten males and fifteen females) were included in this study and considered as control group. Patients with suspected thyroid function disease, or hormonal abnormalities were excluded from the study.

Body mass index is calculated by dividing subjects weight in Kg by their height in m². BMI calculated as:

$$\text{BMI} = \text{weight (kg)} / \text{height (m)}^2$$

Body fat percentage was estimated from person's BMI by the following formula:

$$\text{Body fat \%} = (1.2 * \text{BMI}) + (0.23 * \text{age}) - 5.4 - (10.8 * \text{gender})$$

Where gender is 0 if female and 1 if male.⁽¹¹⁾

Height and waist circumference were measured using the same measuring tape for each parameter.⁽¹²⁾

Biochemical tests were measured for each patient before gastric sleeve followed by another measures one month and then three months after surgery. The same measurements were done for controls.

FBS, HbA1c, lipid profile were measured using enzymatic methods.⁽¹³⁾ HbA1c was measured to approve that the patients were diabetics or not. Fasting Insulin measured using ELIZA kit from RAYBIO (Enzyme-Linked Immunosorbent Assay) while assessment of insulin sensitivity was calculated using the quantitative insulin sensitivity check index (QUICKI) $\text{QUICKI} = 1 / \log(\text{fasting serum insulin}) + \log(\text{fasting glucose})$ where fasting serum insulin is micro units per milliliter ($\mu\text{U/mL}$) and fasting serum glucose is in milligram per deciliter (mg/dl) in the equation.⁽¹⁴⁾ In addition ghrelin hormone measured used ELIZA kit from Phoenix Pharmaceuticals, INC an *in vitro* quantitative assay.

Statistical Analysis

Statistical analysis was carried out using SPSS SPSS-18 (Statistical Package for Social Science – version 18) "PASW Statistics. The results were expressed as numbers, range and mean \pm SE (standard error). Significance of difference was assessed using 2 sample t- test for two independent means and paired t-test for two dependent means. Correlation and regression was applied for the relationship between two quantitative variables, taking $P \leq 0.05$ lowest limit of significance⁽¹⁵⁾.

RESULTS:

Table (1) showed a significant decline in mean values of each of body weight, BMI, WC, fat %, TG, fasting insulin with a significant increase in mean value of QUICKI in patients after one months of LSG compared with mean values of pre-operative group, also there were a significant decline in mean values of body weight, BMI, WC, fat %, total cholesterol, TG, LDL- C, HbA1c and fasting insulin with significant increase in mean value of QUICKI in patients three months post gastric sleeve compared with mean values of pre-operative group, with a significant differences in all studied parameters between patients prior to surgery and controls.

GASTRIC SLEEVE SURGERY

Table 1: Mean ± SEM of BMI, WC, fat %, TC, TG, HDL-C, LDL-C, F.B.S, HbA1c, fasting insulin and QUICKI, in controls and patients one and three months post laparoscopic sleeve gastrectomy versus preoperative condition (base line characteristics).

studied parameters	Controls (mean±SEM) (n=25)	Patients (Mean ± SEM)(n= 24)					
		Pre-operative base line characteristic	One month post-operative measurement	Three months post-operative measurement	P*-Value	P**_-Value	P***_-value
Body weight (kg)	62.53±2.5	131.83± 6.72	117.88± 6.21	109.33± 5.67	0.001(S)	0.001(S)	0.001(S)
BMI(kg/m ²)	22.19 ±0.71	48.02± 1.84	43.05± 1.66	39.72± 1.52	0.03(S)	0.001(S)	0.001(S)
WC (cm)	83.20 ±2.2	101.63± 1.65	98.06± 1.62	96.08± 1.59	0.05(S)	0.001(S)	0.001(S)
Fat percent %	17.67 ±0.99	49.75± 2.13	35.46± 1.99	31.46± 1.82	0.001(S)	0.001(S)	0.001(S)
TC (mg/dl)	172.0 ±3.5	200.51± 5.04	198.32± 3.24	188.04± 2.66	0.43(NS)	0.051(S)	0.001(S)
TG (mg/dl)	121.6 ±4.3	154.81 ±1.95	147.84 ±1.88	142.98 ±1.75	0.05(S)	0.001(S)	0.001(S)
LDL-chol (mg/dl)	102.48± 2.6	114.38 ±3.39	111.77 ±3.08	106.30 ±2.89	0.062(NS)	0.016(S)	0.008(S)
HDL-chol (mg/dl)	60.49 ±1.3	54.03 ±1.64	55.02±1.65	55.83 ±1.63	0.11(NS)	0.073(NS)	0.004(S)
F.B.S. (mg/dl)	90.81 ±2.2	103.79 ±4.01	102.71±3.62	99.33 ±3.11	0.42(NS)	0.071(NS)	0.008(S)
HbA1c %	5.531 ±0.13	6.400 ±0.272	5.638 ±0.159	5.263 ±0.120	0.062(NS)	0.02(S)	0.007(S)
Fasting insulin μIU/ml	6.346 ±0.23	23.183±0.804	14.620±0.518	10.194±0.325	0.04(S)	0.001(S)	0.001(S)
QUICKI	3.2150±0.026	2.74 ± 0.01	2.853 ±0.018	2.97 ±0.01	0.05(S)	0.01(S)	0.05(S)

The data in table (2) showed a significant decrease in mean value of serum ghrelin in patients after one month of LSG compared with mean value of pre-operative group with a significant decrease in mean serum ghrelin three months post LSG compared with mean value of pre-operative group, also the mean serum ghrelin was significantly lower in patients than in controls

Table 2: Mean ± SEM of Ghrelin hormone in controls and in patients prior gastric sleeve, one and three months after surgery.

Ghrelin pg/ml	Controls (n=25)	Patients (n=24)					
		Pre-operative (base line characteristic)	One month post-operative measurement	Three months post-operative measurement	P*-value	P**_-value	P***_-value
	Mean±SEM	Mean± SEM	Mean± SEM	Mean± SEM			
574.3 ±10	457.1 ±9.0	293.39 ±2.46	256.38 ±8.66	0.001(S)	0.001(S)	0.001(S)	

P*: p- value between preoperative (base line characteristic) and one month post-operative measurements.

P**_: p- value between preoperative (base line characteristic) and three months post-operative measurements.

P***_: p- value between patients (pre-operative state) and controls.

S: significant.

NS: non-significant.

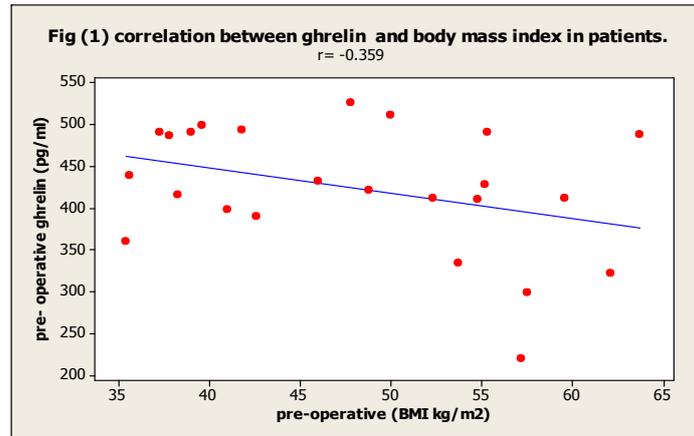


Figure 1: Demonstrated a negative correlation between ghrelin and body mass index between patients prior gastric sleeve and controls ($r = -0.359$)

DISCUSSION:

The occurrence of obesity is increased alarmingly worldwide and is reaching epidemic proportions both in developed and developing countries. Treatment limiting the problem of obesity is an important response to this health, psychosocial and socio-economic health challenge.⁽¹⁶⁾ Gautier T *et al*⁽¹⁷⁾ indicated that weight loss was significantly improved after bariatric surgery (mean loss percentage of excess of body weight, 64.6 % versus 47.1 %) and all reflux symptoms are eliminated without any medication at the end of the follow-up. Bariatric surgery results in an improvement in hyperlipidemia. In a systematic review and meta-analysis, hyperlipidemia improved in over 70% of operated patients. In particular, total cholesterol, low density lipoprotein and triglycerides decreased by an average of 0.86 mmol/L, 0.76 mmol/L and 0.90 mmol/L respectively, while high-density lipoprotein showed no significant change.⁽¹⁸⁾ Hady H R *et al*.⁽¹⁹⁾ found significant differences in insulin and glucose concentrations among patients after LSG. With a statistically significant reduction in insulin. The achievement of normoglycemia after bariatric procedures results from multiple changes that occur postoperatively such as dietary control, decreased plasma ghrelin levels, weight loss, reduction of body fat, and the release of gastrointestinal hormones that interfere with the function of pancreatic β cells (incretins).⁽²⁰⁾ Germain N *et al*⁽²¹⁾ showed that obese individuals have lower ghrelin levels compared with similarly aged people with normal weight. Laparoscopic gastric

sleeve operation “suppresses” Ghrelin levels and thereby reduces appetite and increases weight loss in obese patients. Ghrelin level after LSG is reduced due to the resection of the fundus and body of the stomach, which abates the consumption of carbohydrates and fats. The maintenance of weight loss after gastric sleeve surgery was shown to be due not only to the reduced stomach volume but also to a reduction in ghrelin levels which were no longer elevated before meals, although resection of the fundus may lower ghrelin levels by reducing the volume of ghrelin-producing cells, it has been suggested that the low levels of this hormone after surgery are in fact attributable to the paracrine effect exerted by endogenous gastrointestinal hormones such as glucagon-like peptide-1 (GLP-1).⁽²²⁾ However, it is doubtful that decreased levels of ghrelin are the sole reason for the weight loss achieved by LSG. Zou *et al*.⁽²³⁾ reported the plasma Ghrelin level to show negative correlation with BMI and have no relation with factors such as age and gender in their study on 283 subjects

CONCLUSION:

Ghrelin-producing fundus area is removed with laparoscopic sleeve gastrectomy (LSG), and can say that Ghrelin is a hormone closely linked with obesity taking into account the marked loss in appetite in the period after LSG; the marked suppression of ghrelin levels after LSG is associated with greater appetite reduction and excess weight loss during the first postoperative year, therefore, bariatric surgery may be the treatment of choice for morbid obesity and as the

only one proven in the long-term control of weight loss and represents a promising treatment option in morbidly obese patients.

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GASTRIC SLEEVE SURGERY
