



Plasma ghrelin levels after laparoscopic sleeve gastrectomy in obese individuals

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Background & objectives: Ghrelin is an orexigenic gut hormone expressed by the gastric fundus. Laparoscopic sleeve gastrectomy (LSG) procedure involves resection of the gastric fundus leading to a decreased appetite and weight loss. This study was undertaken to determine the levels of plasma ghrelin after sleeve gastrectomy in obese patients.

Methods: The study was conducted on 90 morbidly obese patients [body mass index (BMI) >40 kg/m²] and severely obese patients (BMI >35/kg/m²) who underwent sleeve gastrectomy. The patients were followed up for six months. Weight loss parameters and plasma ghrelin levels were assessed pre- and postoperatively.

Results: A significant weight loss and decrease in BMI were observed at three and six months postoperatively. A significant decrease in plasma ghrelin levels over six months of follow up postoperatively was also seen.

Interpretation & conclusions: These preliminary findings indicated inhibition of ghrelin production after LSG leading to a decrease in the plasma ghrelin levels within a few days of surgery and sustainable weight loss in obese patients.

Key words Ghrelin - obese - sleeve gastrectomy - weight loss

Obesity is one of the leading causes of morbidity and mortality worldwide. The International Association for the Study of Obesity/International Obesity Task Force, a WHO body has reported that approximately one billion adults worldwide are overweight and another 475 million adults are obese¹. Laparoscopic sleeve gastrectomy (LSG)² has gained popularity as a bariatric procedure due to its safety, low complication

rate and excellent weight loss results. It is a restrictive procedure, involving resection of the gastric fundus, which expresses various hormones associated with hunger and satiety, insulin secretion and energy balance³. LSG appears to permanently inhibit ghrelin production in majority of individuals within days of surgery which is mainly implicated in high success rates of sleeve gastrectomy in obese individuals^{4,5}.

Ghrelin is a 28-amino acid peptide produced from the fundus of the stomach and the proximal intestine^{6,7} and is the only known orexigenic gut hormone. Central and peripheral administration of this hormone leads to increased food intake⁸. Ghrelin levels increase before meals and are suppressed postprandially in proportion to the amount of calories ingested, therefore, suggesting a possible role in meal initiation^{8,9}. Ghrelin stimulates appetite, increases gastric motility and secretion, increases growth hormone secretion and reduces fat utilization⁷⁻⁹. A 24 h profile of ghrelin increases following diet-induced weight loss supporting the hypothesis that ghrelin has a role in the long-term regulation of body weight¹⁰. A few investigators have assessed the change in fasting ghrelin levels after LSG^{4,5,11}. A prospective, double-blind study comparing Roux-en-Y Gastric bypass (RYGB) and LSG confirmed a significant postprandial suppression of ghrelin postoperatively in LSG group while there was no change in the RYGB group¹². Only temporary effects on postoperative plasma ghrelin levels were found by Adami *et al*¹³ in patients who underwent biliopancreatic diversion including sleeve gastrectomy. Schindler *et al*¹⁴ showed an increase in fasting ghrelin accompanied by a paradoxical decrease in hunger after LSG suggesting that weight loss was independent of circulating plasma ghrelin. Thus, the exact role of ghrelin in the pathophysiology of obesity is still under investigation and the establishment of exact correlation between LSG, ghrelin and obesity could be vital for the fight against obesity. The aim of this study was to evaluate the effects of LSG on plasma ghrelin levels and its role in sustainable weight loss in obese patients.

Material & Methods

A total of 90 consecutive patients (52 women and 38 men) aged 24-68 yr who underwent LSG in Dayanand Medical College and Hospital, Ludhiana, India, were enrolled in the study, conducted from August 2013 to June 2015. These included morbidly and severely obese individuals who were suffering from diabetes, hypertension, dyslipidaemia or any one of these diseases. Patients with a history of any bariatric surgical procedure, any terminal illnesses including advanced cancer or end-stage renal, hepatic and cardiopulmonary disease were excluded. Ethical clearance for the study was obtained from the institutional ethics committee and informed written consent were sought from all participants.

Surgical technique: A point on the greater curvature and on the antrum was taken as the starting point

(2 to 10 cm from the pylorus). The lesser sac was entered by opening the gastrocolic ligament. The short gastric vessels and the greater curvature ligaments (gastrosplenic and gastrocolic) were divided by ultrasonic dissection to the left crus. A 32 French bougie was passed transorally into the pylorus, placed against the lesser curvature and then a laparoscopic stapler was introduced along the length of the bougie. Stomach was separated and removed with the help of ports¹⁵. A drain was then placed along the stapler line.

The patients were subjected to follow up for six months postoperatively and weight loss parameters such as body mass index (BMI) were measured. Fasting plasma ghrelin levels were also measured using the enzyme-linked immunosorbent assay (ELISA)¹⁶. Fasting venous blood samples (1 ml) were collected in pre-chilled tubes-containing aprotinin/ethylenediaminetetraacetic acid (EDTA) solution preoperatively on day 1 of hospital admission, one week, three and six months following the operation and the samples were analyzed for plasma ghrelin levels using ELISA kit (Ghrelin EIA kit-sigma RAB0207 Merck KGaA, Darmstadt, Germany).

Statistical analysis was performed to compare the means among the groups using Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, IBM Corp., Version 20.0. Armonk, NY, USA). A one-way repeated measures analysis of variance (ANOVA) was conducted to evaluate the null hypothesis that there was no change in the plasma ghrelin levels pre- and postoperatively at one week, three months and six months following LSG.

Results & Discussion

A total of 90 patients (mean age 46.27±11.17 yr) were included in the study. Mean height and mean weight were 1.614±0.105 m and 131.24±15.42 kg, respectively. Mean BMI was 49.25±3.96 kg/m². BMI and weight loss showed a significant reduction in three months which sustained until six months postoperatively ($P<0.001$).

A one-way repeated measures ANOVA was conducted to evaluate the null hypothesis that there was no change in the plasma ghrelin levels pre- and postoperatively at one week, three and six months following LSG in obese patients. There was a significant decrease in plasma ghrelin levels at one week, three months and six months postoperatively following LSG ($P<0.001$) compared to pre-operative levels (Table).

Table. Effect on weight loss parameters and fasting plasma ghrelin levels

Parameters	Pre-operative	Post-operative 1 week	Post-operative 3 months	Post-operative 6 months
Weight (kg)	131.24±15.42	127.34±14.73	112.10±12.44***	90.00±10.5***
Weight loss (kg)	-	3.9±1.52	21.22±3.98***	41.68±10.54***
Body mass index (kg/m ²)	49.25±3.96	47.63±3.87	41.55±2.98***	32.43±2.05***
Fasting plasma ghrelin (pg/ml)	42.49±18.17	22.29±10.3***	18.45±8.9***	19.36±8.6***

Data are presented as mean±SD. P***<0.001 compared to pre-operative level

Alterations of orexigenic hormone ghrelin play an important role in appetite fluctuation and preservation of achieved weight reduction following bariatric surgery^{15,17}. Various factors play a role in causing weight loss following LSG such as decreased gastric capacity, decreased gastric emptying time and reduced ghrelin levels postoperatively¹⁸. In our study, the mean weight loss and BMI following LSG at one week, three and six months postoperatively were significant ($P<0.001$) (Table). Gluck *et al*¹⁹ also reported similar results. This was also in concordance with other studies^{4,5}.

Being a short-term follow up this study may not reflect long-term effects on weight loss produced by LSG. The sample size was also small. The findings need to be studied on a larger group before these can be standardized and recommended.

In conclusion, a significant decrease in fasting plasma ghrelin levels was seen after LSG, a surgical intervention for treatment of morbid obesity, which began as early as the first week and remained till six months postoperatively. A significant weight loss and reduction in BMI following the surgery were also observed.

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Conflicts of Interest: None.

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