Ghrelin concentration before and after bariatric surgery

Oleg Galimov[1*], *Vladislav* Khanov[1], *Kseniya* Nasirova[1], *Dmitriy* Galimov[1], *Tel'man* Ibragimov[1], *Tatyana* Titova[1], *Anastasiya* Titova[1], *Robert* Ziangirov[1], and *Rinat* Sufiyarov[1]

[1] Bashkir State Medical University, 450008 Ufa, Russia

Abstract. Introduction. Aim of the work is to study the concentration of ghrelin before and after bariatric gastric surgery in patients with morbid obesity. Materials and methods. A study of ghrelin levels was carried out in 25 patients with morbid obesity who underwent restrictive bariatric surgery (13 gastroplications and 12 "sleeve resections" of the stomach). Results and discussion. The initial level of ghrelin in the blood in patients with morbid obesity was lower compared to the levels determined with normal body weight. We did not observe the expected decrease in ghrelin levels during resection of the fundic ghrelin-producing part of the stomach. Conclusion. A clinical study shows that changes in gastric volume after restrictive bariatric interventions (sleeve resection or gastropplication) are accompanied by a slight increase in blood ghrelin levels; this increase is greater the higher the percentage of body weight loss after surgery. Deeper study of this area will help identify new strategies for treating morbid obesity in the future.

1 Introduction

The prevalence of overweight and obesity is increasing worldwide, and this trend will continue in the coming years. Obesity is a risk factor for many diseases such as diabetes, cardiovascular disease and others [1, 2, 3, 4]. Most researchers now recognise that conservative treatment of extreme degrees of obesity is an extremely difficult task and for 90-95% of patients is not feasible [5, 6]. Many authors, assessing the rapid growth in the number of obese patients and the significant increase in the costs of their treatment, justify the need to use a powerful resource of various surgical methods to correct the pathological changes inherent in obesity [7, 8, 9].

Understanding the mechanisms of the influence of ghrelin on obesity can lead to the development of effective prevention and treatment strategies, contributing to the maintenance of overall health. Ghrelin is a hormone produced in the stomach that plays an important role in the regulation of appetite and metabolism. Its effects on the body can have a significant impact on various aspects of obesity [10, 11]. Ghrelin, often referred to as the "hunger hormone" which stimulates the feeling of hunger. Elevated ghrelin levels can lead to increased food intake, which in turn can contribute to the accumulation of excess weight.

* Corresponding author: galimovov@mail.ru

Studies show that ghrelin levels may be inversely proportional to body weight. Underweight people often have elevated ghrelin levels, while ghrelin levels may decrease in overweight or obese individuals. This may explain why some people have difficulty losing weight [12, 13, 14].

In the structure of bariatric surgeries, considering the risks of complications and the performance technique, restrictive interventions are the most popular, among them gastric sleeve resection and gastroplication [15, 16, 17]. At the same time, many authors attribute the pathophysiological mechanism of excess weight loss after surgery to a decrease in the level of ghrelin in the patient's organism.

2 Materials and methods

Clinical and laboratory studies were performed in patients with morbid obesity (MO) on the basis of the Clinic of Surgical Diseases and New Technologies with a course of Institute of Medical Education of the Federal State Budgetary Educational Institution of Higher Professional Education "Belarusian State Medical University" of the Ministry of Health of Russia. At present the Clinic has experience in performing various invasive bariatric procedures in 288 patients whose BMI exceeded 35 kg/m2. In recent years, preference has been given to the use of restrictive techniques, and in particular, sleeve resection of the stomach, performed mainly laparoscopically. An alternative to sleeve gastric resection, aimed at reducing the volume of the organ, is the operation of gastric apposition (gastroplication). We have proposed a new method of laparoscopic gastroplication in surgical treatment of patients with morbid obesity (patent for invention RF № 2654572). The essence of the technique is to reduce the volume of the stomach by means of turning (invagination) into its lumen with the help of special instruments a part of the stomach wall (creating a fold by means of corrugating serous-muscular sutures) along the whole stomach. In this case, the volume of the stomach is significantly reduced, and the patient begins to feel the feeling of satiety when eating much faster than it was before the operation. The technical result is achieved by the fact that the stomach after its mobilisation along the large curvature with the help of a specially designed tool - intestinal clamp is rolled into a tube in the form of a "roll" and fixed with a non-absorbable thread. A special calibration gastric probe is used to reduce the stomach volume to 50 ml [18].

The ghrelin level was studied in 25 morbidly obese patients who underwent restrictive bariatric surgeries (13 gastroplications and 12 "sleeve resections" of the stomach). The content of ghrelin in blood serum was determined by competitive enzyme immunoassay using ELISA Kit for Ghrelin (GHRL) for human according to the protocol of the reagent manufacturer Cloud-Clone Corp. (PRC). The functional state of various organs was evaluated in dynamics by routine clinical and laboratory tests. Statistical processing of the results was performed using Statistica 6.0 application software package. We calculated the median (Me), interquartile intervals [25%, 75%]. Statistical significance of intergroup differences in mean values was assessed using the Mann-Whitney U-test. Pearson's correlation analysis was used to identify the relationship between the signs. Differences were considered statistically significant when $p \leq 0.05$.

3 Results and discussion

The average plasma ghrelin concentration in humans, including both active and inactive forms, is known to range from approximately 500 to 700 pg/ml in normal body weight and from approximately 200 to 400 pg/ml in obesity. Ghrelin levels were studied in 25 morbidly obese patients who underwent restrictive bariatric surgery (13 gastroplications and 12 gastric

sleeve resections) between 1 and 4 years (mean 2.5±1.5 years). In all patients who underwent restrictive interventions the effect of body weight reduction was obtained in different degrees. In addition, 5 morbid obese patients who refused surgical treatment and 10 patients with normal body weight treated in the clinic for diseases not related to obesity were examined as a comparison group. All patients were comparable in terms of gender, age, baseline BMI. Investigations for recurrence of obesity were done. Ethical committee of the clinic approved all procedures and protocols and written informed consent was obtained from all subjects before inclusion in the study. The results of the study are summarised in Table 1.

Table 1. Key indicators for the assessment of the main criteria in the clinical groups

	Age (years)	gender		Body weight (kg)	BMI ref (kg/m^2)	BMI final (kg/m^2)	Decrease in BMI (%)	Ghrelin ref (pkg/ml)	Ghrelin final (pkg/ml)
		M	F						
Sleeve resection (n=12)	45.6±4.8	3	11	109±2.5	48.5±8.8	30.0±1.5	24.4±1.5	330±25	440±25
Gastroplication (n=13)	42.9±2.4	5	8	99.8±5.6	35.7±1.6	29.4±1.5	17.4±1.5	350±25	450±25
Normal weight Control (n=10)	48.0±4.1	4	6	82.5±5.2	25.4±0.9	25.4±0.9	-	650±25	-
Treatment cons. (n=5)	47.8±4.7	2	3	106±5.5	48.2±5.2	47.4±5.8	-	350±25	-

The results showed that changes in gastric volume after restrictive bariatric interventions (whether sleeve resection or gastroplication) were accompanied by a slight increase in serum ghrelin levels. The highest ghrelin values (more than 450 pkg/ml) were observed in 3 patients after sleeve resection and 3 after gastroplication, who achieved the greatest weight loss. It is noteworthy that when comparing patients' answers to the quality-of-life questionnaire (SF-36), morbidly obese patients noted a positive effect of surgical treatment on the physical component of health and social functioning, indicating a reduced role of physical problems in limiting life activity, while no correlation with the mental component was found.

4 Conclusion

The reference level of ghrelin in the blood of morbidly obese patients was lower compared to the values determined at normal body weight. We did not observe the reduction in ghrelin levels expected with resection of the fundal ghrelin-producing part. This clinical study shows that ghrelin levels are not significantly increased in subjects who have undergone gastric volume changes after restrictive bariatric interventions (gastroplication or sleeve resection). Apparently, the increase in its concentration in the serum of patients in the postoperative period along with the decrease in body weight can explain the "hunger feeling", depression, and other mental disorders after the operation. Pathophysiological mechanisms of body weight loss after restrictive surgeries, including both resection of gastrin-producing zone and gastroplication, are obviously primarily related to the reduction of stomach volume. The loss of mass can be explained by restriction of food passage in compliant patients. Patients need a potential trigger for weight loss, which is the bariatric procedure. In this case, medical restrictions are initially based on the fear of developing a postoperative complication and subsequently reasoned dietary recommendations. The successful result of the operation associated with a significant loss of excess body weight comes when new eating habits and new principles of physical and social behaviour are formed, regardless of the technique of the restrictive surgery performed. This proves the necessity of a multidisciplinary approach including participation of psychiatrist, nutritionist, endocrinologist and rehabilitologist in determining the indications, choice of operative technique and postoperative rehabilitation of bariatric patients. The mechanism of high adipose tissue catabolism after bariatric surgery

is poorly understood, but enzymatic and hormonal changes in the body may play a crucial role. Understanding the influence of ghrelin on obesity holds promise for the development of new therapies. Current research is focused on investigating whether drug approaches or dietary strategies can be used to regulate ghrelin levels to manage appetite and weight.Further research in this area will help to better understand the mechanisms of ghrelin's effects and develop effective methods of weight control.

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