The role of bariatric surgery and appetite-related hormones metabolism in obesity treatment: a literature review

A. O. Nykonenko, Ye. I. Haidarzhi, O. S. Nykonenko, M. H. Holovko, A. S. Protsenko

Zaporizhzhia State Medical University, Ukraine

The most frequently performed surgical interventions in the treatment of obesity are the laparoscopic sleeve gastrectomy (LSG), laparoscopic greater curve plication (LGCP), laparoscopic Roux-en-Y gastric bypass (RYGB). Along with effective weight loss, these operations lead to changes in the production of appetite-related hormones that play an important role in the endocrine regulation of energy metabolism.

The aim was to learn the role and interaction of the above-mentioned bariatric operations (LSG, LGCP and RYGB) and appetite-related hormones (ghrelin, leptin, adiponectin) metabolism in obesity treatment using scientific literature data with considering famous obesity surgeons’ point of view.

Materials and methods. The current review was conducted by searching the following databases in Internet: PubMed, Scopus and Google Scholar, using combination of keywords for the bariatric surgery and appetite-related hormones metabolism.

Results. Our review shows that the above-mentioned surgeries (LSG, LGCP, RYGB), aimed to the treatment of obesity, directly lead to a decrease in body mass index and weight loss and, indirectly, through the adipose tissue function, have different significant effects on energy balance and appetite-related hormones levels. The anatomical and physiological changes described in the review are most likely caused by the above-mentioned surgical procedures.

Conclusions. Nowadays LSG, LGCP and RYGB are the most effective operations in obesity treatment with a strong similarity. There is a close interaction between BMI and fat tissue loss, caused by above-mentioned bariatric surgery, with appetite-related hormones levels. However, the surgical effects on this process in each case have been not enough studied and requires further work in this direction.

Key words: obesity, bariatric surgery, appetite-regulating hormone.

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E-mail: nikonandra@gmail.com
Introduction

Nowadays, morbid obesity is one of the most common diseases in the world and represents a global problem for the world’s population [1,2]. In recent years, there has been a significant increase in the number of patients suffering from overweight and obesity, which is reaching of epidemic proportions and requires action to address the problem [3]. According to the literature, more than 1.9 billion people aged over 18 are overweight, with 600 million of them are obese of varying severity [4]. As an important component of the metabolic syndrome, the presence of obesity significantly increases the risk of the dangerous diseases and conditions such as type II diabetes mellitus, hypertension, coronary heart disease, osteoarthritis, sleep apnea, nonalcoholic fatty liver, rectum, colon, pancreas cancers, dyslipidemia, and related, often fatal, cardiovascular complications [3,5–9]. In view of this, the treatment of obesity is becoming more widespread [10–12]. Currently, treatment of obesity successfully amenable to bariatric surgery, and the proportion of surgical techniques has steadily increased [13–18]. Today, the most frequently performed surgical interventions in the surgical treatment of obesity are the laparoscopic sleeve gastrectomy (LSG), laparoscopic greater curve plication of the stomach (LGCP), laparoscopic gastric bypass (RYGB) [2,9,19–24]. Such operations are quite effective in a significant reduction in the body mass, a decrease in blood cholesterol and glucose levels and are associated with low rates of surgical complications [24–28]. At the same time, these surgical interventions change the levels of appetite-related hormones (ghrelin, leptin and adiponectin) due to various technical aspects, which play a great role in energy metabolism [29–37]. The role of these anatomical and physiological effects in obesity treatment have not been enough investigated and continue to be discussed by obesity surgeons.

The aim

The aim of this work was to study the role and interaction of the above-mentioned bariatric operations (LSG, LGCP and RYGB) and appetite-related hormones (ghrelin, leptin, adiponectin) metabolism in obesity treatment using scientific literature data with considering famous obesity surgeons’ point of view.

Materials and methods

The current review was conducted by searching the following databases: PubMed, Scopus, and Google Scholar. We use combination of keywords relating to bariatric surgery and appetite hormones metabolism: bariatric surgery, metabolic syndrome, appetite hormones, laparoscopic sleeve gastrectomy, laparoscopic greater curve plication, laparoscopic Roux-en-Y gastric bypass, ghrelin, leptin and adiponectin. The publications in English language from 1998 to the present day were included. All founded duplicate articles were removed, topics and abstracts of the articles were reviewed and irrelevant studies were excluded.

Results

Nowadays, the endocrine status of adipose tissue is of particular interest. Studies show that adipose tissue is highly active endocrine organ that produces a number of hormones involved in the regulation of energy metabolism, among which leptin, ghrelin and adiponectin deserve special attention [38].

Leptin – adipose tissue hormone responsible for satiety and plays an important role in the regulation of body weight [39]. Leptin is produced mainly by adipocytes and acts as a link between adipose tissue and hypothalamic centers, although its products are seen in other organs and tissues: the bottom area of the stomach, skeletal muscle, liver, placenta [40,41]. This hormone acts on the central nervous system by inhibiting food intake and stimulating the feeling of hunger and energy expenditure. The level of leptin is directly proportional to the amount of adipose tissue. In patients with anorexia the level of leptin is sharply reduced, and increases in weight gain. Mutations in the gene encoding leptin or its receptor cause pathological neuroendocrine dysfunction and obesity [42–44]. In addition, a decrease in leptin level leads to a decrease in matrix metalloproteinase – 8, which leads to a remission of diabetes mellitus in obese patients [45]. This proved that leptin is a specific marker of weight loss, fat mass loss and its decreasing level can denote effectiveness of bariatric surgery [28]. After bariatric surgery, the size of the adipocytes decreases and the expression of leptin increases. Thus, the function of adipocytes is modified, which consists in an improved transfer of leptin [46].
Ghrelin is one of the most important proteohormones involved in the formation of hunger. The physiological feeling of hunger during a negative energy balance is a primitive survival function, the centers of which are located in the older parts of the brain — the hypothalamus and the hindbrain. The sense of appetite for hedonic food, based on a sense of taste, smell, appearance, appears in the mesolimbic system and the frontal cortex of the brain. These systems are closely intertwined. A more progressive hedonic system can become dominant in this interaction. So, hormone ghrelin is able to change the hedonic perception of food and convey a sense of desire to use it even with a positive energy balance [47]. This can explain the obesity epidemic, associated with a bias in the production of foodstuffs with an attractive appearance, taste, smell. Hedonic systems become dominant, thereby increasing the feeling of hunger, and homeostatic systems remain stable [48]. Simultaneously, several other hormones has a significant effect on appetite and energy balance. Ghrelin is synthesized from prohormone in mucosal epithelial cells of gastric fundus and only a small part of this hormone is synthesized in the placenta, kidney, pituitary and hypothalamus [49,50]. A number of studies have confirmed the effect of prohormone (unacylated) ghrelin, which is more than 90 % of total ghrelin, on the sensitivity of cells to insulin, metabolism, muscle regeneration and protection of β-cells [51,52]. Large numbers of the receptors to ghrelin are found in adipose tissue, which emphasizes its role in the regulation of energy metabolism [53]. According to studies, ghrelin stimulates food intake and hunger center, strengthens the peristalsis of the stomach, accelerating its emptying, thus causing the urge to eat [54,55]. An interesting fact is that ghrelin is significantly increased in patients on a low-calorie diet, and stomach bypass surgery reduces the content of ghrelin in plasma [56,57]. This confirms the notion that ghrelin concentration may be in direct correlation with the stomach size and the different types of operations for gastric surface areas: restriction differently may influence its plasma concentration, and thus the metabolic processes in the body related to obesity treatment and weight loss [58–60].

In addition to the above-mentioned hormones, adipose tissue secretes adiponectin — collagenous protein known as adipocyte-specific hormone that affects carbohydrate and fat metabolism [61–63]. The role of this protein in the plasma is varied, and its effects on the organs and tissues are sufficiently wide [64]. The most important of them are the reduction of insulin resistance and lowering blood glucose levels as well as anti-inflammatory and antiatherogenic effects [65–68]. The level of adiponectin decreases in obesity, thereby reducing insulin sensitivity and increasing the risk of cardiovascular diseases [69,70]. A number of studies have revealed a certain dependence of the adiponectin level on body weight changes: with a slight increase in body weight the level of adiponectin increases and a significant increase in body weight (10–15 %) does not change the hormone level. In addition, an increase in body weight, characterized by the term «obesity» leads to a decrease in the adiponectin level. Thus, there is a certain threshold effect of the adiponectin level changing as a function of body weight [71,72].

Analysis of literature data showed, that the most frequently performed surgical interventions in the surgical obesity treatment, which affect weight loss and metabolism of appetite hormones, are the laparoscopic sleeve gastrectomy (LSG), laparoscopic greater curve plication of the stomach (LGCP), laparoscopic Roux-en-Y gastric bypass (RYGB) [2,3,8,12,24,73–76]. Due to the surgical technique peculiarities for various types of these operations, one or another effect on body weight reduction and changes in metabolism of appetite hormones that play an important role in the successful obesity and metabolic syndrome treatment is achieved.

So, at LSG the tube is formed from the stomach by its resection along the greater curvature to decrease food intake and reduce body weight associated with it [77]. RYGB is a bypass operation in which a small gastric pouch is formed and most of the digestive stomach is excluded. Thus, the food goes from the esophagus directly into the formed small gastric pouch, and then is drained into the small intestine, i.e., bypassing the duodenum, gets directly into the distal small intestine [78]. Gastric bypass surgery provides significant weight loss with minimum complications [79]. LGCP is a restrictive bariatric procedure without gastrectomy [80]. The innovation of LGCP raised some question about its effectiveness compared to traditionally used techniques such as LSG [76]. LGCP is a novel technique avoiding stomach resection – the gastric volume reduction is performing due to invagination and cross linking of its walls (plication) [24,73,76,80]. Another advantageous feature of LGCP is its reversibility. The greater curve of stomach is sutured vertically in rows to reduce its volume and distention. This facilitates obese patients to intake less food with early satiety. The results showed that the LGCP procedure is very safe, effective, feasible and efficient with comparable early results to other restrictive procedures with minimal morbidities [8,24,74–76,80].

Table 1. The results of BMI before and after operation

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>LSG</td>
<td>44.9 ± 3.4</td>
<td>29.6 ± 4.1</td>
<td>Kehagias I. 2011</td>
</tr>
<tr>
<td></td>
<td>45.1 ± 3.6</td>
<td>29.0 ± 3.6</td>
<td>Karamanakos S.N., 2008</td>
</tr>
<tr>
<td></td>
<td>44.7 ± 1.6</td>
<td>32.0 ± 1.04</td>
<td>Woelnerhanssen B., 2011</td>
</tr>
<tr>
<td></td>
<td>44.7 ± 5.3</td>
<td>32.0 ± 5.0</td>
<td>Peterli R., 2012</td>
</tr>
<tr>
<td></td>
<td>44.6 ± 3.5</td>
<td>30.48 ± 4.29</td>
<td>Talebpour M., 2017</td>
</tr>
<tr>
<td>LGCP</td>
<td>48.39 ± 4.89</td>
<td>30.13 ± 2.73</td>
<td>Talebpour M., 2017</td>
</tr>
<tr>
<td></td>
<td>40.7</td>
<td>34.6 ± 6.3</td>
<td>Khidr N., 2017</td>
</tr>
<tr>
<td></td>
<td>43.7 ± 5.7</td>
<td>32.9</td>
<td>Brethauer S.A., 2011</td>
</tr>
<tr>
<td></td>
<td>38.0 ± 3.1</td>
<td>32.5 ± 3.8</td>
<td>Atlas H. et al., 2013</td>
</tr>
<tr>
<td></td>
<td>43.0 ± 4.9</td>
<td>34.7 ± 6.11</td>
<td>Nykonenko et al. 2016</td>
</tr>
<tr>
<td>RYGB</td>
<td>45.8 ± 3.7</td>
<td>31.3 ± 3.9</td>
<td>Kehagias I. 2011</td>
</tr>
<tr>
<td></td>
<td>46.6 ± 3.7</td>
<td>31.5 ± 3.4</td>
<td>Karamanakos S.N., 2008</td>
</tr>
<tr>
<td></td>
<td>47.6 ± 2.0</td>
<td>31.1 ± 2.2</td>
<td>Woelnerhanssen B., 2011</td>
</tr>
<tr>
<td></td>
<td>47.6 ± 6.8</td>
<td>31.16 ± 7.5</td>
<td>Peterli R., 2012</td>
</tr>
<tr>
<td></td>
<td>46.2 ± 0.6</td>
<td>34.9 ± 0.8</td>
<td>Nestor De La Cruz-Munoz, 2013</td>
</tr>
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</table>
Obzory

Table 2. The indicators of appetite-related hormones levels before and after operation

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Hormone</th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>LSG</td>
<td>Ghrelin</td>
<td>127.5 ± 96.9 ng/l</td>
<td>87.5 ± 59.1 ng/l</td>
<td>Marek Bužga, 2014</td>
</tr>
<tr>
<td></td>
<td></td>
<td>610.15 (440.8–775.0) pg/ml</td>
<td>342.0 (316.1–445.6) pg/ml</td>
<td>José Manuel Ramón, 2012</td>
</tr>
<tr>
<td></td>
<td></td>
<td>76.8 ± 43.7 pmol/L</td>
<td>41.8 ± 11.3 pmol/L</td>
<td>Kalinowski P., 2017</td>
</tr>
<tr>
<td></td>
<td>Leptin</td>
<td>44.2 ± 3.3 ng/mL</td>
<td>20.4 ± 2.8 ng/mL</td>
<td>B. Woelnerhanssen et al., 2011</td>
</tr>
<tr>
<td></td>
<td></td>
<td>43.6 ± 11.9 μg/l</td>
<td>24.3 ± 13.3 μg/l</td>
<td>Marek Bužga, 2014</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.8 ± 1.8 nmol/L</td>
<td>1.5 ± 1.0 nmol/L</td>
<td>Kalinowski P., 2017</td>
</tr>
<tr>
<td></td>
<td>Adiponectin</td>
<td>6.3 ± 0.4 pg/mL</td>
<td>9.6 ± 1.0 μg/mL</td>
<td>B. Woelnerhanssen et al., 2011</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14.5 ± 8.8 ng/l</td>
<td>24.8 ± 12.0 mg/l</td>
<td>Marek Bužga, 2014</td>
</tr>
<tr>
<td>LGCP</td>
<td>Ghrelin</td>
<td>127.5 ± 86.9 ng/l</td>
<td>20.1 ± 10.1 ng/l</td>
<td>marek Bužga, 2015</td>
</tr>
<tr>
<td></td>
<td>Leptin</td>
<td>53.6 ± 14.9 μg/l</td>
<td>23.3 ± 12.1 μg/l</td>
<td>marek Bužga, 2015</td>
</tr>
<tr>
<td></td>
<td>Adiponectin</td>
<td>16.3 ± 7.8 mg/l</td>
<td>25.8 ± 11.0 mg/l</td>
<td>marek Bužga, 2015</td>
</tr>
<tr>
<td>RYGB</td>
<td>Ghrelin</td>
<td>584.0 (403.0–645.4) pg/ml</td>
<td>730.0 (611.0–866.7) pg/ml</td>
<td>José Manuel Ramón, 2012</td>
</tr>
<tr>
<td></td>
<td></td>
<td>74.6 ± 32.4 pmol/L</td>
<td>130.2 ± 124.3 pmol/L</td>
<td>Kalinowski P., 2017</td>
</tr>
<tr>
<td></td>
<td>Leptin</td>
<td>45.7 ± 3.3 ng/mL</td>
<td>16.2 ± 4.5 ng/mL</td>
<td>B. Woelnerhanssen et al., 2011</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.6 ± 1.6 nmol/L</td>
<td>1.3 ± 1.1 nmol/L</td>
<td>Kalinowski P., 2017</td>
</tr>
<tr>
<td></td>
<td>Adiponectin</td>
<td>5.6 ± 0.7 μg/mL</td>
<td>11.2 ± 1.5 μg/mL</td>
<td>B. Woelnerhanssen et al., 2011</td>
</tr>
</tbody>
</table>

Modern situation in surgical treatment of obesity shows that all operations (LSG, LGCP, RYGB) due to anatomical and physiological changes in the digestive system caused by the above mentioned technical aspects, along with effective weight loss and associated reduction in adipose tissue mass, lead to changes in the production and synthesis of hormones that are produced in adipose tissue and involved in the endocrine regulation of energy metabolism [64]. A number of studies have confirmed that the normalization of the hormonal profile in patients suffering from obesity occurs due to the reduction in the adipose tissue amount and does not depend on the method of surgical intervention [87]. Marek Bužga et al., 2014, 2015, José Manuel Ramón et al., 2012, B. Woelnerhanssen et al., 2011, marked significant changes in the levels of appetite hormones (leptin, adiponectin and ghrelin) and anthropometric indicators like weight and BMI after LSG, LGCP and RYGB. In their studies, all patients attained effective weight loss and different changes in ghrelin, leptin and adiponectin levels after bariatric surgery (LSG, LGCP, RYGB) [83,88–91] (Table 2).

Our review showed that leptin level has the tendency to decrease after different types of bariatric operations [88–91]. The changes in ghrelin levels are controversial after different types of bariatric surgery. A number of long-term studies have shown that in RYG and LSG operations a comparable reduction in patient body weight occurs, but the ghrelin level increases in RYG and decreases in LSG. Therefore, the level of ghrelin does not affect weight loss [88,90,91]. Surgery-mediated modulation of brain function via modified postoperative secretion of gut peptides and vagal nerve stimulation was identified as an underlying mechanism in weight loss and improvement of weight-related diseases. Increased basal and postprandial plasma levels of gastrointestinal hormones like glucagon-like peptide-1 and peptide YY that act on specific areas of the hypothalamus to reduce food intake, either directly or mediated by the vagus nerve, are observed after surgery while suppression of meal-induced ghrelin release is increased [92].

B. Woelnerhanssen et al., 2011, Marek Bužga et al. 2014, 2015 showed a tendency to increase in adiponectin levels in all patients after different types of bariatric surgery until the 12-month follow-up period that proves the effectiveness of bariatric surgery in reduction of insulin resistance, lowering blood glucose levels and treatment of diabetes mellitus.

Thus, adipose tissue is not an inert organ and may have functions over and beyond its role in energy depot in the body. Our review shows that fatty tissue — an endocrine organ, playing an important role in a number of hormones secretion (leptin, ghrelin, adiponectin) and their receptors, involved in metabolic processes. The above-mentioned surgery (LSG, LGCP, RYGGB), aimed to obesity treatment, lead to a decrease in fat mass, through the adipose tissue function, indirectly have different effects on energy balance and result in weight loss. However, their effects on the process in each case have not been enough studied and requires further work in this direction.

Conclusions

Our study showed that nowadays LSG, LGCP and RYGGB are the most effective and safe operations in obesity and metabolic syndrome treatment with a strong similarity.

Important metabolic role of appetite hormones (ghrelin, leptin and adiponectin) in the development of obesity is sometimes controversial and at the present stage remains insufficiently studied.

The technical aspect of LSG, LGCP and RYGGB effect on the metabolism of appetite hormones is not sufficiently clear and further study of this effect is essential.

Successful surgical treatment of obesity is impossible without extensive knowledge of the most common obesity surgeries technical aspects (LSG, LGCP and RYGGB) and their effects on metabolic changes and appetite hormones levels (leptin, ghrelin and adiponectin).

Thus, the further studies of the bariatric surgical operations (LSG, LGCP and RYGGB) effectiveness and the role of appetite hormones (leptin, ghrelin and adiponectin) metabolism in the obesity treatment with greater sample size and longer follow-up period are necessary.
References


