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CHOLECYSTOKININ METABOLIC PROFILE IN POST-BARIATRIC PATIENTS

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Abstract

Objective: To describe the metabolic effect of cholecystokinin and its relationship with post-bariatric sugery patients.

Methodology: This is a qualitative analysis in the form of integrative literature review, the theme chosen clearly and explicitly: "What is the metabolic profile of cholecystokinin and its effect on post-bariatric sugery patients?". After formulating the guiding question, the following keywords in Portuguese, English and Spanish were chosen: "bariatric surgery", "bariatric surgery", "cirugía bariátrica"; "cholecystokinin", "cholecystokinin", "cholecystokinin"; "fome", "hunger", "hambre"; "satiety response", "satiety response", "respuesta de saciedad", "Roux-en-Y anastomosis", "anastomosis Roux-en-Y", and "anastomosis en-Y de Roux", through the combination of the controlled descriptors, Medical Subjetc Heading (MeSH) and the Health Science Descriptors (DeCS) resources, as well as the Boolean operators "AND" and "OR". In the databases Latin American and Caribbean Literature on Health Sciences (LILACS), Virtual Health Library (VHL), PubMed, Scientific Electronic Library Online (SciELO) and Google Scholar, a search for clinical trials conducted in humans from 2012 to 2022 was performed.

Results: 2,038 articles were identified. The final sample of this review consisted of eleven scientific articles; of these, four were found in the VHL database, two in PubMed, and five in Google Scholar. Thus, concepts about the digestion process and the hormones involved, bariatric surgery techniques and their hormonal effects, were observed in each of the selected articles.

Conclusions: Cholecystokinin, a gastrointestinal hormone, is one of the major endocrine satiety signals. It is observed that with gastroplasty, the levels of the hormone CCK are elevated; thus, besides increasing satiety, cholecystokinin aids in weight loss. Therefore, bariatric surgery is highly effective in improving the patient's quality of life.

Keywords: Cholecystokinin, obesity, bariatric surgery

1.0 INTRODUCTION

Obesity is a health problem belonging to the group of chronic non-transmissible diseases, characterized by excessive accumulation of body fat. Currently, it is considered an important public health problem due to its

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association with several diseases, such as locomotor disorders, respiratory difficulties, and dermatological problems. It can also cause more serious diseases, such as dyslipidemias, type 2 diabetes, cardiovascular diseases, and certain types of cancer (1).

Obesity has multifactorial causes and is the result of interactions between genetic, metabolic, social, behavioral, and cultural factors. It is caused mainly by high calorie intake combined with a sedentary lifestyle, which favors the storage of adipose tissue generated by the positive energy balance, since the amount of energy acquired is greater than that spent (2).

The use of drug treatments for morbid obesity is not very effective, with a failure rate of about 90%. Thus, other forms of treatment have been developed, including surgical treatment, which is considered promising, mainly because of the significant and lasting weight reduction (3).

Bariatric surgery, also known as gastroplasty, is the main surgical intervention in the treatment of morbid obesity, in situations in which it was not possible to reduce weight or the risks of other health problems by traditional methods, such as diets, clinical treatments, and physical exercises (4). This procedure is based on the reduction of the stomach in up to 20 cm3, which can reach a reduction of 90% of its absorption capacity. And, consequently, the stomach starts to support a smaller capacity of food, filling up quickly and transmitting the satiety message to the brain, which results, in turn, in a lower intake of food (5).

Associated with the satiety process is cholecystokinin (CCK), which is a hormone produced mainly by the L cells of the duodenum and jejunum. Its bioactive forms originate from the selective cleavage of an amino acid precursor (pro-CCK), generating the forms CCK-8, CCK-22, CCK-33, and CCK-58, the numerical suffix indicating the amount of amino acids that are present. The CCK-33 form of this hormone is widely distributed in the gastrointestinal tract and can be found in the hypothalamus (6).

The plasma concentration of CCK is increased right after a meal, activates receptors present in the vagus nerve, and remains elevated for up to five hours after eating. Diets with a higher concentration of proteins or fats stimulate the release of the hormone, generating the feeling of satiety in a more intense way than when compared to a predominantly carbohydrate diet (7).

Studies bring the relations between evaluations of the levels of intestinal peptides and hormones in the periods before and after bariatric surgery. In the case of cholecystokinin, for example, its amount increases or remains unchanged in the postoperative period, assisting in post-meal satiety and in the reduction of food intake and, consequently, for weight loss.(8)

In view of what has been presented, the present scientific production proposes to describe the metabolic effect of cholecystokinin and its relationship with post-bariatric patients.

2.0 METHODOLOGY

This article is a qualitative analysis in the form of an integrative literature review, which, according to Botelho LLR. et al (2011), has as its main objective to trace an analysis of the knowledge already built in previous research on a given

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topic. In order to begin the study, a guiding question was developed that synthesizes the chosen theme in a clear and explicit way: "What is the metabolic profile of cholecystokinin and its effect on post-bariatric patients?". Subsequently, the keywords in Portuguese, English and Spanish were chosen: "bariatric surgery", "bariatric surgery", "cirugía bariátrica"; "cholecystokinin", "cholecystokinin", "cholecystokinin"; "fome", "hunger", "hambre"; "satiety response", "satiety response", "respuesta de saciedad", "anastomosis em-Y de Roux", "anastomosis Roux-en-Y" and "anastomosis en-Y de Roux", by combining the Medical Subjetc Heading (MeSH) controlled descriptors and the Health Science Descriptors (DeCS) resources, as well as the Boolean operators "AND" and "OR".

The articles and studies selected were searched exclusively in the Latin American and Caribbean Literature on Health Sciences (LILACS), Virtual Health Library (VHL), PubMed, Scientific Electronic Library Online (SciELO), and Google Academic databases, among which 2,038 results were identified. After formulating the guiding question, the following inclusion and exclusion criteria were applied.

Inclusion criteria were: articles written in Portuguese, Spanish and English, published between 2012 and 2022, theses, dissertations and full articles, and clinical studies conducted only in humans. And the exclusion criteria were: review articles, studies conducted in animals and that were not available in full for free. After that, the articles were downloaded to be read in full in order to extract the information to feed the tables in the Microsoft Excel program.

3.0DISCUSSION AND RESULTS

The final sample of this review consisted of twelve scientific articles, selected by the previously established inclusion criteria. Of these, five were found in the VHL database, five in PUBMED, and five in Google Scholar. Chart 1 shows the specifications of each of the articles.

Table.1. Data from the articles

Article Title	Source database	Authors	Year	Type of study
"Appetite and bariatric surgery."	Academic Google	Coelho, Joana Patrícia Gonçalves.	2018	Dissertation
Association between jet lag and metabolic, anthropometric and food intake response in patients undergoing bariatric surgery: an observational	Academic Google	Carvalho, Aline Cunha.	2019	Dissertation

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and longitudinal study".				
Metabolic and nutritional effects of protein supplementation in women with weight regain after 24 months of bariatric surgery: a randomized clinical trial".	Academic Google	Gomes, Daniela Lopes.	2015	Randomized Clinical Trial
"Endocrine implications of obesity and bariatric surgery".	BVS.	Dyaczyóski, Michael et al	2018.	Integrative review.
"Fasting and Meal-Induced CCK and PP Secretion Following Intragastric Balloon Treatment for Obesity".	BVS.	Mathus-Vliegen, EMH, de Groot, GH	2013	Randomized Clinical Trial
"Gastrointestinal Hormones, Intestinal Microbiota and Metabolic Homeostasis in Obese Patients: Effect of Bariatric Surgery".	BVS.	A Federico, M Dallio, S Tolone, AG Gravina, V Patrone, et al.	2016	Prospective study.
"Ghrelin, CCK, GLP-1, and PYY (3-36): Secretory Controls and Physiological Roles in Eating and Glycemia in Health, Obesity, and After RYGB".	BVS.	Steinert, Robert E., et al.	2017	Integrative review.
"Weight loss and satiety-related	Academic Google	Meireles, Ana Sofia Bessa.	2018.	Monograph

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hormonal variations".				
"Biochemical profile of women with weight regain in the late postoperative period of bariatric surgery".	Academic Google	Coelho, Giovana de Aguiar.	2015	Monograph
"Postprandial Nutrient Handling and Gastrointestinal HormoneSecretion After Roux-en-Y Gastric Bypass vs Sleeve Gastrectomy".	PubMed	Svane, Maria S et al.	2019	Cross-sectional study.
"Responses of gut and pancreatic hormones, bile acids, and fibroblast growth factor-21 differ to glucose, protein, and fat ingestion after gastric bypass surgery".	PubMed	Jensen, Christian Zinck, et al.	2020	Randomized Clinical Trial

SOURCE: AUTHORS

In this context, concepts about the digestion process and the hormones involved, bariatric surgery techniques, and their hormonal effects are discussed.

Obesity

According to the World Health Organization (WHO), overweight and obesity are defined as an abnormal or excessive accumulation of fat that can damage health. To classify an adult individual as overweight or obese, the most commonly used tool is the Body Mass Index (BMI), which relates weight to height. According to the WHO, an individual is overweight if he/she has a BMI of 25 kg/m2 or more, and obese if his/her BMI is over 30 kg/m2 (10).

Worldwide, the prevalence of obesity has almost tripled since 1975 (10). Therefore, the WHO officially declared morbid weight problems as an international epidemic in 1997. (10) In 2016, more than 1.9 billion adults (39%)

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over the age of 18 were overweight and of these, more than 650 million (13%) were obese. Having an increased BMI is a major risk factor for chronic non-communicable diseases such as cardiovascular disease, diabetes, joint disease, and some types of cancer (10). It is likely that the increasing prevalence of obesity is due to factors related to genetic background, some disease of the hypothalamic-gastrointestinal axis, and/or the current environment and lifestyles such as reduced need for physical exertion in occupations and easy access to highly palatable foods (10, 2).

A common feature of obesity is the weakening of the postprandial response to food intake of satiety-related hormones, such as GLP-1 and PYY, which may be associated with decreased satiety and increased food intake. Also, leptin and ghrelin levels do not seem to follow the expected behavior in obese individuals. Increased leptin levels and decreased ghrelin levels may reflect a situation of leptin resistance and ghrelin hypersensitivity in these patients, changes that also impair satiety regulation (10). Therefore, these factors together contribute to higher caloric intake and consequent body weight gain (13).

Secretion of gastrointestinal hormones and their physiological parameters

There is a complex neurohormonal system that controls body weight; homeostatic regulation of food intake occurs through central integration of signals in the arcuate nucleus of the hypothalamus, the brainstem, and parts of the cortex and limbic system, with satiety signals reaching the brain via the circulation or via the vagus nerve (10).

Some hormones, such as cholecystokinin (CCK), glucagon like peptide-1 (GLP-1), peptide YY (PYY), ghrelin, insulin, and leptin, can be released by the digestive tract (from stimuli such as gastric distension gastric emptying, and/or nutrient sensing by enteroendocrine cells) or by adipose tissue and perform anorexigenic actions - except ghrelin, which performs orexigenic actions (10, 13). In addition, synergistic interactions between different sites in the gastrointestinal tract also contribute to secretion (11).

The digested nutrients activate specific nutrient receptors and transporters expressed on the apical surface of enteroendocrine cells, leading to secretion of CCK, GLP-1 and PYY on the basolateral side of the cells. From this, four modes of action can occur. In the classical endocrine mode, the hormones diffuse from the lamina propria into the mesenteric capillaries, which drain into the hepatic-portal vein and, in turn, into the systemic circulation, allowing hormonal action on distant targets. In the neuroendocrine mode, lamina propria hormones activate vagal afferents, which stimulate brain-mediated responses. In the paracrine mode, lamina propria hormones act on receptors on nearby cells, either neuroendocrine cells or other types of cells. Although ghrelin secretion is not directly stimulated by nutrients, it can act in these modes (12).

Furthermore, GI motor function influences endocrine function, since gastric emptying and intestinal transit determine which enteroendocrine cells are exposed to the chyme and for how long, which affects hormone secretion. Gastric

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emptying patterns are affected by meal volume, pressure, energy density, macronutrient digestibility, and adaptation (12).

For most meals, nutrient sensing from the small intestine inhibits ghrelin secretion and stimulates secretion of CCK, GLP-1, and PYY. In turn, ghrelin stimulates and CCK, GLP-1 and PYY inhibit gastric emptying. In addition to decreasing the emptying of liquid meals, GLP-1 stimulates pyloric tonic and phasic pressures and reduces duodenal pressure waves. The relationship of these feedback loops to satiety is complex because, depending on the circumstances, acceleration of gastric emptying can decrease satiety by decreasing gastric volume signals or increase satiety by increasing postgastric signals (12).

Besides accelerating gastric emptying and increasing intestinal motility, ghrelin, which is secreted by the stomach, pituitary gland, and small intestine, stimulates appetite, since it boosts the reward system by acting on the dopaminergic pathways and hypothalamic nuclei. In contrast, GLP-1 and PYY are secreted by the enteroendocrine L-cells and the former induces satiety by indirect stimulation of pro-opiomelanocortin (POMC) and the latter inhibits gastric acid secretion and exocrine pancreatic function, stimulates enterocytes, decreasing appetite and increasing satiety. And, in central mechanisms, PYY decreases NPY expression and releases POMC as well.(16)

Thus, gastric emptying, which controls the rate at which the ingested food appears in the small intestine, intestinal transit, the rate of digestion, and the detection of nutrients in the small intestine are the main determinants of the inhibition of ghrelin secretion and the stimulation of CCK, GLP-1, and PYY during and after meals. And these hormones contribute to three processes that regulate meal initiation and meal size: hunger, which refers to the energizing process by food acquisition and meal initiation; satiety, which leads to meal completion; and postprandial satiety, which inhibits eating after meals and prolongs the interval between meals (12).

In addition, there are other hormones involved in the satiety process, such as insulin, which is produced by the β-cells of the pancreas and released after each meal and also plays an important role in controlling glucose hemostasis, avoiding hyperglycemia (19). there is also leptin, which is produced predominantly in the adipose tissue, and circulates in levels proportional to body fat levels, suppresses food intake by stimulating appetite suppressor neurons and inhibiting orexigenic neurons in the brain, controls energy expenditure, signals insulin, and stimulates lipogenesis (10).

Action of cholecystokinin

CCK cells are open type cells, that is, their apical surfaces are exposed to the intestinal lumen. They are not only a single species of I-cells, in fact, enteroendocrine CCK cells also express and secrete ghrelin, GLP-1, PYY, GIP, neurotensin or secretin. Enteroendocrine CCK cells are densely expressed in the

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duodenum and proximal jejunum, less dense in the distal jejunum, and sparse in the ileum (12).

Mixed nutrient meals increase CCK secretion. Oral lipids stimulate CCK secretion by more kcal, whereas proteins are intermediate and carbohydrates stimulate CCK secretion less. Cholecystokinin circulates predominantly in the 58 amino acid form (CCK-58) and its plasma levels increase within 10 to 15 minutes (12).

Intraluminal nutrients stimulate directly - via nutrient receptors expressed on the apical surface of CCK cells - and indirectly the secretion of cholecystokinin - via CCK release factors "pancreatic monitor peptide" and "intestinal luminal CCK release factor" (12). This peptide is released in the duodenal and jejunal mucosa about 15 to 30 minutes after food ingestion (16).

CCK delays gastric emptying through vagal-vagal reflexes stimulated by endocrine and paracrine signaling. In addition, CCK contributes to the increase in tonic and phasic pyloric pressures and in reductions in antral and duodenal pressures stimulated by intraduodenal lipids - which explains its role in gastric emptying (12).

The vagal-vagal gastric accommodation reflexes are triggered primarily by mechanoreceptors and intestinal nutrient receptors and are mediated in part by CCK. These reflexes increase gastric volume as meals progress, preventing significant increases in intragastric pressure or gastric wall tension. With the lack of stimulation of gastric tension receptors, gastric accommodation does not present with aversive sensations, only a pleasant feeling of fullness (12).

Cholecystokinin is the best established GI endocrine satiety signal in humans and may contribute to meal-related glucose control both indirectly, through its effect on gastric emptying, and directly through control of hepatic glucose production via vagal reflex. In a study of intra-meal effects, plasma CCK increased more during meals in women than in men, but ratings of hunger and satiety did not differ (12).

Some defects in CCK signaling can lead to obesity. For example, human CCKAR receptor polymorphisms are associated with increased meal size, increased food intake, and obesity. In addition, allele variations in CCK were significantly more prevalent in obese people who habitually ate very large meals (12).

Bariatric surgery

Bariatric surgery is considered an option in the treatment of obesity associated with improved quality of life, cardiovascular profile, and several other comorbidities, such as type 2 diabetes mellitus and sleep apnea, since it helps in reducing body weight and controlling metabolic homeostasis through changes in serum profiles of gastrointestinal hormones. (2+16) Bariatric surgery can be performed in patients with BMI> 40 kg/m2 or in patients with BMI> 35kg/m2 with associated obesity-related comorbidities who have been unable to lose weight

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through lifestyle interventions. This has been shown to be the most effective method of treating obesity in the long term (10). However, also in the long term, weight regain may be associated with reduced production of anorexigenic incretins (13). Therefore, more studies are needed to have a better knowledge about the mechanisms involved in the changes after the surgical intervention.

In a study of 19 obese preoperative patients, it was found that parameters for metabolic syndrome and insulin resistance improved significantly after surgery. Other biochemical variables, including fasting glucose, triglycerides, cholesterol, LDL-cholesterol, and HDL-cholesterol levels improved significantly. In particular, preoperatively, all patients met the criteria for insulin resistance, and postoperatively, all patients normalized their HOMA value. Fasting plasma glucose levels were also normalized in all ten diabetic patients 6 months after surgery. Twelve patients who were hypertensive and hypercholesterolemic before surgery had normalization of blood pressure and cholesterol levels after surgery. In addition, all preoperative hypertriglyceridemic patients had normalized parameters after surgery.(19)

Types of bariatric surgery

There are several types of bariatric surgery: gastric banding, gastric sleeve (SG), bilio-pancreatic bypass, duodenal switch, and Roux-en-Y gastric bypass (RYGB). The goal of bariatric surgery is to cause a marked reduction in energy intake, triggering an early and increased feeling of satiety by reducing hunger signals, as well as (in mixed techniques) bypassing important parts of the digestive tract, promoting rapid food transit, which results in partial malabsorption. In this review, only two types of bariatric surgery will be focused on, the RYGB and the SG (10).

RYGB is restrictive and malabsorptive surgery, in which the gastric volume is reduced by creating a small gastric pouch with a capacity of only 15-30ml near the gastroesophageal junction and a gastrojejunal anastomosis, thus diverting nutrients directly from the stomach into the proximal jejunum. Thus, the mechanisms of RYGB involve the combination of reduced stomach size, changes in gastrointestinal motility due to increased gastric emptying (10)-resulting in accelerated macronutrient absorption-, neuronal changes, and increased hormone secretion, (11) due to nutrient redirection and anatomical reorganization. (10,13) This surgical technique promotes a large and durable weight loss and remission of type 2 diabetes and other obesity-related comorbidities in most patients (11).

SG is a restrictive procedure only. It is a partial gastrectomy of the stomach's fundus and body, which gives rise to a tubular structure whose size and shape resembles that of a banana. Its effects are caused by metabolism that involves favorable changes at the level of neurohormonal changes due to the resection of the stomach, and at the level of increased speed of gastric emptying (10).

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In summary, these two surgical procedures induce slightly different changes in hormonal patterns over time, although in terms of weight loss, BMI, and glycemic control they produce comparable effects (10).

Hormonal effects in post-bariatric patients using the RYGB technique

RYGB and related bariatric surgery procedures substantially decrease ghrelin secretion and increase secretion of CCK, GLP-1, and PYY by rapidly increasing nutrients in the small intestine, especially in the first few months after surgery (12, 13, 14). This postprandial enhancement of key gut hormones is essential for the beneficial effects after RYGB (11, 13).

Due to the reduced gastric lumen, only a fraction of the normal gastric volume can be accommodated and antral trituration and pyloric control of gastric emptying are absent post RYGB. As a result, RYGB accelerates gastric emptying of liquids and solids (although emptying of small solid meals with volumes no larger than the volume of the volsa may be slower). This, in turn, often leads to bloating, nausea, and dumping in RYGB patients (12).

After bariatric surgery, CCK levels increased postprandially in reflex to mixed food, probably by parasympathetic nerve avivation. Thus, the increase in CCK levels contribute to the progress of satiety and glucose homeostasis after RYGB(2) and it is possible to observe an improvement in anxiety, sexual behavior, sleep, memory and intestinal inflammation.(16) But another work did not find any kind of changes in this parameter after RYGB(10). Another study shows that proximal derived cholecystokinin (CCK) and glucose-dependent insulinotropic polypeptide (GIP) show less pronounced changes (11).

GLP-1 and PYY responses are up to 10 times higher than in non-operated people (11). Therefore, post-prandial plasma values of both GLP-1 and PYY are significantly increased in the very first week after this type of bariatric surgery (10), which can be explained by the direct delivery of nutrients to more distal segments of the small intestine, such as glucose, that can be absorbed already in the Roux limb and be responsible for the early and greater response of GLP-1, PYY (11, 14). Thus, increased secretion of GLP-1 and PYY cumulatively contributes to increased perception of satiety and provides a reduction in food and energy intake (10).

Most studies describe a significant reduction in fasting plasma levels of ghrelin, since the area that secretes this hormone is also reduced, which may contribute to the success of the surgery, since low levels will not cooperate with the feeling of hunger, reducing the appetite of the operated patients.(20) However, there are other studies that show no significant changes and still others that show a significant increase. Therefore, the results are not consistent. According to the differences, it is suggested that the effect of surgery on plasma levels of ghrelin depends on the portion of the gastric fundus affected by the surgical procedure (10).

Fasting leptin levels after RYGB bariatric surgery decrease significantly and continue to decrease progressively with weight loss. As for insulin levels, it

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is likely that there is a decrease in the resistance to its action (1 week after the intervention), which reflects in a rapid improvement of glycemic control even before the occurrence of significant weight loss and also an improvement of insulin sensitivity either hepatic or peripheral during the first two years after RYGB and beta cell function (10).

Regarding the effects of glucose, protein, and fat intake in patients by RYGB, it was observed that cholecystokinin responses were higher after protein intake, which may be explained by accelerated amino acid absorption in the exposed segments of the more distal small intestine, which also contain amount of CCK-secreting I-cells. Furthermore, compared with control subjects, RYGB subjects had higher total PYY and GIP responses after glucose and GLP-1 after all meals, while GIP and CCK responses were lower after fat. The ghrelin responses did not differ between meals or between groups (11).

Hormonal effects in post-bariatric patients by SG technique

It was observed that cholecystokinin levels increase after SG - more markedly than in RYGB. And, also similar to what happens in RYGB, the values of GLP-1 and PYY after SG are exaggeratedly secreted in the postprandial period, which can be explained by the accelerated gastric emptying and the early contact of enteroendocrine cells with the chyme. Thus, these hormones contribute to significant appetite suppression (10, 14).

Studies show that fasting and postprandial plasma levels of ghrelin are significantly reduced soon after bariatric surgery using the SG technique and that this decrease remains stable over time and is much more prominent than in other types of bariatric surgery. Therefore, it contributes to a great suppression of appetite, which can be justified by the fact that, in this surgical intervention, the gastric fundus, the main site of ghrelin production in the human body, is resected (10, 14).

It is also observed that plasma concentrations of leptin are significantly reduced after the first post-operative SG and tend to continue decreasing as the operated patients proceed with weight loss. And, as for fasting insulin levels, as with BYGR, a decrease and an increase in sensitivity to its action also occurs, even before significant weight loss occurs (10).

4.0 CONCLUDING REMARKS

In conclusion, cholecystokinin, a gastrointestinal hormone, is one of the major endocrine satiety signals, contributing to several health-related factors. In view of the above, it is observed that the hormonal effects in post-bariatric patients also depend on the technique used in surgery.

Thus, gastroplasty, a surgical procedure performed in obese patients, in addition to reducing the stomach area, also raises the levels of the hormone CCK, increasing satiety levels and strongly assisting in weight loss. Although some patients have problems after the surgery, even so, bariatric surgery is highly effective and indicated to fight obesity and improve the quality of life of the

population in question. And it is essential to emphasize the importance of further studies in the area so that this issue can be better understood by all.

REFERÊNCIAS

1. Schwab U, Lauritzen L, Tholstrup T, Haldorssoni T, Riserus U, Uusitupa M, Becker W. Effect of the amount and type of dietary fat on cardiometabolic risk factors and risk of developing type 2 diabetes, cardiovascular diseases, and cancer: a systematic review. Food Nutr Res. 2014;58. doi: 10.3402/fnr.v58.25145. eCollection 2014
2. Mathus-Vliegen EM, de Groot GH. Fasting and meal-induced CCK and PP secretion following intragastric balloon treatment for obesity. Obes Surg. 2013 May;23(5):622-33. doi: 10.1007/s11695-012-0834-6. PMID: 23224567
3. .Mingrone G, Panunzi S, De Gaetano A, Guidone C, Iaconelli A, Capristo E, et al. Metabolic surgery versus conventional medical therapy in patients with type 2 diabetes: 10- year follow-up of an open-label, single-centre, randomised controlled trial. Lancet [Internet]. 2021;397(10271):293–304. Available from: http://dx.doi.org/10.1016/S0140-6736(20)32649- 0
4. - Ryder JR, Gross AC, Fox CK, Kaizer AM, Rudser KD, Jenkins TM, et al. Factors associated with longterm weight-loss maintenance following bariatric surgery in adolescents with severe obesity. Int J Obes [Internet]. 2017. Disponível em: http://www.ncbi.nlm.nih.gov/pubmed/ 28894289%0Ahttp://www.nature.com/doifinder/10.1038/ijo.2017.193
5. Yoshino M, Kayser BD, Yoshino J, Stein RI, Reeds D, Eagon JC, et al. Effects of Diet versus Gastric Bypass on Metabolic Function in Diabetes. N Engl J Med. 2020;383(8):721– 32.
6. Sociedade Brasileira de Cirurgia Bariátrica e Metabólica 2017. Disponível em https://www.sbcbm.org. br/tecnicas-cirurgicas-bariatrica
7. Santos KN dos, Colli LFM. OS RISCOS DOS INIBIDORES DE APETITE: A SIBUTRAMINA. Rease [Internet]. 30º de setembro de 2021 [citado 3º de abril de 2022];7(9):794-807. Disponível em: https://www.periodicorease.pro.br/rease/article/view/2281
8. Hubert PA, Papasavas P, Stone A, Swede H, Huedo-Medina TB, Tishler D, et al. Associations between Weight Loss, Food Likes, Dietary Behaviors, and Chemosensory Function in Bariatric Surgery: A Case-Control Analysis in Women. Nutrients, v. 11, n. 4, 2019. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/30970617/>. Acesso em: 03 abr. 2022.
9. Dirksen C, Jorgensen NB, Bojsen-Moller KN, Kielgast U, Jacobsen SH, Clausen TR, et al. Gut hormones, early dumping and resting energy expenditure in patients with good and poor weight loss response after Roux-en-Y gastric bypass. Int J Obes (Lond). 2013; 37(11):1452-9.
10. Dyaczyński M, Scanes CG, Koziec H, Koziec H, Pierzchała-Koziec K. Endocrine implications of obesity and bariatric surgery. Endokrynol Pol. 2018;69(5):574-597. doi: 10.5603/EP.2018.0059. PMID: 30379322.

11. Botelho, L. L. R., de Almeida Cunha, C. C., & Macedo, M. (2011). O método da revisão integrativa nos estudos organizacionais. *Gestão e sociedade*, *5*(11), 121-136.
12. Meireles, A. S. B. (2018). Perda ponderal e variações hormonais relacionadas com a saciedade.
13. JENSEN, Christian Zinck et al. Responses of gut and pancreatic hormones, bile acids, and fibroblasto growth factor-21 differ to glucose, protein, and fat ingestion after gastric bypass surgery. **American Journal of Physiology-Gastrointestinal and Liver Physiology**, v. 318, n. 4, p. G661-G672, 2020.
14. STEINERT, Robert E. et al. Ghrelin, CCK, GLP-1, and PYY (3–36): secretory controls and physiological roles in eating and glycemia in health, obesity, and after RYGB. **Physiological reviews**, v. 97, n. 1, p. 411-463, 2017.
15. CARVALHO, Aline Cunha et al. Associação entre jet lag social e resposta metabólica, antropométrica e do consumo alimentar de pacientes submetidos à cirurgia bariátrica: um estudo observacional e longitudinal. 2019.
16. COELHO, Joana Patrícia Gonçalves. Apetite e cirurgia bariátrica. 2018.
17. SVANE, Maria S. et al. Postprandial nutrient handling and gastrointestinal hormone secretion after Roux-en-Y gastric bypass vs sleeve gastrectomy. **Gastroenterology**, v. 156, n. 6, p. 1627-1641. e1, 2019.
18. Gomes, D. L. (2015). Efeitos metabicos e nutricionais da suplementação proteica em mulheres com reganho de peso ap ól ós 24 meses de cirurgia bariátrica: Um ensaio clínico randomizado
19. FEDERICO, Alessandro et al. Gastrointestinal hormones, intestinal microbiota and metabolic homeostasis in obese patients: effect of bariatric surgery. **in vivo**, v. 30, n. 3, p. 321-330, 2016