ORIGINAL ARTICLE

Paradigm of Remission of Diabetes Mellitus Type 2, through the New Physiological Mechanisms of Metabolic Surgery

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ABSTRACT

Background: Type 2 diabetes mellitus (DM2) is a major public health challenge we face today. It is the first cause of disability and is associated with the main causes of death in our country. In Mexico City, it was reported that 79% of diabetic patients did not have optimal levels of hemoglobin 1c (HbA1c) (<6.5%), while 47% are not properly controlled (HbA1c >9%). Metabolic surgery is the best treatment option for Type 2 diabetes, yet the mechanisms involved are presumed not traditionally considered. **Objective:** The objective of the study was to provide an update of the mechanisms involved in the remission of DM2 following metabolic surgery. **Methods:** Systematic review of literature, using mesh terms, until December 31, 2018, 105 articles considered encountering pertinent. **Results:** DM2 remission after surgery depends on complex interactions between the microbiota, biliary acids, and intestinal epithelium, more over than malabsorption or restrictive processes. Bipartition of intestinal transit constitutes a surgical option based on the physiologic principles of responsible remission of diabetes, and it is a simple and the most secure procedure for the management of diabetes. Mechanisms include restoration/enhancement of incretin secretion; as well as an improvement of bile acid concentration and manipulation microbiome, rather than the commonly accepted restriction and malabsorption. Intestinal transit bipartition is a novel and simple procedure that complies with the current mechanisms involved, with comparable results in terms of safety and efficacy with the more complex and demanding techniques, such as gastric bypass. **Conclusions:** Metabolic surgery is the best treatment for DM2 in terms of remission and prevention of complications, modifying secretion of enterohormones, the concentration of biliary acids, and the modification of microbiota.

Key words: Diabetes mellitus type 2, gastrointestinal transit, incretins, intestine small, metabolic surgery, surgical procedures

INTRODUCTION

Diabetes mellitus Type 2 (DM2) is the main public health challenge we face today, it is the leading cause of disability and is associated with the leading causes of death in our country. In Mexico City, it was reported that >79% of diabetic patients have optimal hemoglobin 1c (HbA1c) (<6.5%), while 47% have significant lack of control (HbA1c> 9%).[1]

Surgery is the best treatment, in terms of decreased HbA1c glucoside, blood glucose control, induction of remission, and prevention of the development of microvascular complications.[2] Both cited bariatric and metabolic procedures favor improvement in 89.2% of patients and up to 64.7%, the remission of the disease.[2] Both in morbidly obese patients and those with a body mass index (BMI) <35 kg/m^2[3] and even, in overweight patients (BMI <30 kg/m^2).

In Mexico, according to the clinical practice guidelines for surgical treatment of DM2 in adults with BMI of 30 to 34.9 kg/m^2, they are considered as candidates for surgical treatment patients with HbA1c >8% while other authors

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include diabetic patients with difficult control, even with a BMI below 30 kg/m^2. Both (malabsorptive/restrictive) were considered appropriate surgery techniques restrictive bariatric and mixed bariatric.

Although many authors equate the terms "bariatric" and "metabolic," there are substantive differences between these procedures by themselves. Bariatric surgery is focused on weight loss and narrow your target restricts intake (adjustable gastric band and intragastric balloon), sleeve gastrectomy (SG) or processes still considered as mixed: Gastric bypass and laparoscopic Roux (Laparoscopic Roux-en-Y Gastric Bypass, Gastric Miniderivation (Mini-gastric Bypass) duodenal-ileostomy with anastomotic (Single Anastomosis Duodenum-Ileal); Distal Loop Duodenum-Ileostomy, biliopancreatic and duodenum-jejunostomy (Djos), etc.

Although bariatric procedures restrictive response may decrease cardiometabolic risk factors, control of diseases such as DM2 is marginal; there are reports with 3% remission completed prolonged in patients undergoing adjustable gastric band and between 0% and 3% in those undergoing SG. Metabolic surgery, on the other hand, proposes the re-establishment of the kinetics of enterohormones without using restriction prosthesis, or stenosis or favor malabsorption, that is, why the reason for them, indicated for DM2 with difficult control, in patients without obesity.[4]

In Mexico, gastric bypass and Laparoscopic Roux has proven to be a safe and effective option to improve the metabolic profiles in non-obese diabetic patients with a complete remission rate of 47.4% while 36.8% achieved remission partial with an index of 13% complications.[5] Among the most frequent complications are cholecystolithiasis (13–36%), hypoglycemia after derivation (1–13.3%),[6] intestinal obstruction (4.4%), upper gastrointestinal bleeding, reduce of bone density, and nutritional complications.[7]

It is important pointing that the small intestine is the site of principal absorption of certain nutrients, segmental exclusion achieved with gastric bypass and Laparoscopic Roux, biliopancreatic derivation, duodenal-ileostomy with an anastomosis, the duodenum jejunostomy, and other procedures favor micronutrient deficiencies, Vitamins A, C, D, and K, thiamin, folic acid, iron, selenium, zinc, and copper.

Therefore, usually, supplements Vitamin B[12] required (1,200 g), calcium carbonate (1000 mg), Vitamin D 3 (1000U), and ferrous sulfate (300 mg), which must readjust according to serum levels. Other major disadvantages of gastric bypass Laparoscopic Y Roux Count on personnel specifically trained for this procedure, as well as an infrastructure that is not common in hospitals secondary care, making it available option to consider other procedures.

Bipartition of intestinal transit is the simplest metabolic cited exercise to practice with which manages to get the changes necessary to promote the secretion of incretins.[8] Increasing exposure to intestinal epithelial bile acids and also modify the microbiota without promoting malabsorption. Although the concept is not new, our knowledge about has deepened to ensure that these procedures can be safer and less invasive.[9]

The aim of this study was to provide an update on mechanisms involved in remission of DM2 after metabolic surgery.[9]

MECHANISMS RESPONSIBLE FOR THE REMISSION OF DIABETES BY METABOLIC SURGERY

Caloric restriction and weight loss are two common interventions bariatric restrictive, malabsorptive, and mixed results. However, it has been shown that the metabolic control favored by restrictive surgery is not ideal for maintaining remission of DM2 strategies.[10]

Over the past decade, it has been established that the most important factors to promote such referral are the neurohormonal changes affecting the regulation of energy, appetite, glucose homeostasis; induced changes in microbiota, and changes in the metabolism of bile acids and their interactions with X farsenoid (FXR) receptor in addition to changing patterns of diet and exercise.[11]

Diet

It is undeniable that patients undergoing a surgical procedure most frequently modify their dietary habits than those they do not do it. Besides such to caloric intake, macronutrient concentrations, and glucose or fructose content is determined in the natural history of diabetes during post-operative as sustained hyperglycemia decreases insulin secretion. It has proven the importance of diet because with more fat and protein, promotes complete remission of diabetes up to 42–100% of patients.[12]

Moreover, the supercharging favors the proliferation of intestinal epithelium, with increased earlier absorption of nutrients. Furthermore, it emphasizes stress endoplasmic reticulum on, which favors proinflammatory state, insulin resistance, and decreased insulin production, including dysfunction and beta-cell apoptosis and aggravating glucotoxicity, which latter effects insulin and other fermentable carbohydrates that help shape the microbiota, and the concentration of butyrate and propionate.

INCRETINS, DECRETINS, AND DIABETES AS A POOR INTESTINAL ADAPTATION

Incretins are hormones secreted by the intestinal epithelium which promote secretion of insulin in response to swallowing

and exposure to bile acids, as a result of interactions with intestinal microbiota. Glucagon-like peptide-1 (GLP-1) is a peptide incretin produced by L cells located in the terminal ileum and proximal colon, from the proteolisis of preproglucagon; it has a half-life of about two minutes, as it is "inactivated" by dipeptidyl peptidase 4 (DPP-4) the DPP-4 (7-36).[15-17] The primary form of GLP-1 (7-36), controls the release of insulin dependent on glucose and optimizes the function of beta cells, in addition to inhibit glucagon secretion, delay gastric emptying and promote satiety. In addttion, it is metabolize and transformed into GLP-1 (9-36) reestablishing antral motility blocked by GLP-1 (7-36), while GLP-1 (28-36) 18-20 inhibits liver production of glucose and stress oxidation in the hepatocyte, and GLP-1 (32-36) modulates the metabolism of glucose all around the body. Hence, comprehensive treatment of this patients is an indispensable condition procedural success.[21]

The diet interacts with patients and his microbiota, modifying its conformation and the production of butyrates, propionates, products of fermentation of carbohydrates (prebiotics) and free fatty acids; they interact through the TGR5 receivers, FFARs / SCFA-R, TLR and TR of the L cells of distal intestine, to favor the production of incretins, such as the GLP-1 peptide and the YY peptide, changing the eating pattern, satiety, insulin secretion and survival or pancreatic regeneration

Vegetables contain substances called thylakoids preferably located in the chlorinated chloroplasts that independently promote the secretion of the peptide and promoting satiety. Another important factor associated with intake is that vegetables contain insulin-dependent glucose and optimizes the function of the beta cells, also inhibit glucagon secretion, delay gastric emptying, and promote satiety. When metabolized, it becomes GLP-1 (9–36) re-establishing antral motility blocked by GLP-1 (7–36), while the GLP-1 (28–36)[22,23] inhibited hepatic glucose production and oxidative stress in hepatocytes and GLP-1 (32–36) modulates glucose metabolism throughout the body.

The reduced concentration of peptide GLP-1 is involved in the pathophysiology of various diseases considered characteristic of the western lifestyle. Treatment with these incretin analogs improves control of DM2, arterial hypertension, myocardial remodeling, dyslipidemia, obesity, albuminuria, steatohepatitis, etc. Metabolic surgery and bariatric mixed procedures increase incretin concentrations GLP-1 to promote early contact of the terminal ileum with nutrients, improving metabolic conditions of patients, then decrease concentrations and peptide- C due to decreased glucose.

The GLP-1 peptide promotes the proliferation of beta cells, insulin sensitivity, cardioprotection, improves heart function, promotes neuroprotection and neuroproliferation, and improves cognitive function.[24]

Apparently, these incretin mechanisms contribute to satiety, and the hedonic value of food intake of high fat and carbohydrates, as well as motivation for ingestion through dopaminergic pathways in the reward centerstimulation;Secreting cholecystokinin (CCK).[27]

The alterations of incretins kinetics, produce a delayed reaction and reduction, and are an initial factor in the pathophysiology of obesity and DM2. Reset proper secretion, as achieved by stimulating early form in the distal ileum with procedures such as gastric bypass laparoscopically Roux, the duodenum-jejunostomy, the duodenum-ileostomy distal handle, and ileal interposition bipartition and intestinal transit, is a condition sine qua non to promote and maintain remission of DM2. The glucose-dependent insulinotropic peptide, (GIP), is another incretin, secreted by K cells of the duodenum and jejunum, improve insulin secretion and promotes proliferation of pancreatic beta cells.

Oxyntomodulin (OXM) is cosecreted with GLP-1 and PYY peptides, decreased food intake, gastric emptying, and exocrine pancreatic secretion by activation of the glucagon receptor, the GLP-1 or both, and increases the basal energy expenditure.

Polypeptide YY is another enterohormone created by L cells (1–36), in which metabolized intervenes dipeptidase DPP-4 (3–36). The main function is in the hypothalamus, decreasing food intake, and also gastric secretion, pancreatic, and intestinal. Hormone ghrelin inhibits neuropeptide Y and in the arcuate nucleus through the Y2 receptor, the activation of proopiomelanocortin (POMC) cells. The release can be increased by the ingestion of prebiotics like inulin, as fermentation products of carbohydrates can increase their expression and interactions in the hypothalamus.

Interrupting YY polypeptide, GLP-1, and insulin secretion by octreotide administration, increases the reward associated with food intake, addition reactions, and anticipatory hedonic ingestion.

Other sites of expression of GLP-1, PYY, and GIP peptides, and hormones such as neurotensin and ghrelin, are enteroendocrine cells.

DM2 AND POOR ADAPTATION INTESTINAL

The anatomical and functional characteristics of the small intestine have not been able to adapt to the changes that have occurred in the conditions laid dietary from the neolithic revolution and have increased in the last 50 years.

It has been linked to increased intestinal longitude with pathological conditions such as obesity, diabetes, and dyslipidemia. The length of the intestine from healthy individuals selected for transplantation is approximately 356 cm, while in patients with obesity and dyslipidemia is 500 cm, and in diabetics, up to 760 cm on average. However, some authors have associated intestinal length *in vivo,* measured by enteroscopy, with height and thus the weight and BMI. Found intestinal lengths 261–755 cm, using different measurement methods.[28,29]

It has been described the number of replacements and the L cells, production of GLP-1, PYY, and OXM peptides in the terminal ileum, and is equal in patients sufficient healthy and those with diabetes. Therefore, it cannot be ruled out or discard that intestinal length, along with the composition of the microbiota and kinetics of bile acids, is a contributing factor to the development of inappropriate kinetics of incretin and the consequent development of obesity and diabetes.[30]

Decretins

The neurohormones decretins are produced in the foregut (duodenum and jejunum proximal) and its functions are to decrease insulin secretion and block the mechanisms of satiety. There is still much controversy about the role of decretins. For example, some authors have shown that U neuromedin, a neuropeptide expressed in the central nervous system, it helps to reduce food intake and body weight by acting on receptors 2 (NmUR2)[30] while receptors 1 (NmRU1), expressed in pancreatic tissue, inhibit insulin secretion and the mechanisms of satiety.[31-33] It has even been suggested that neuromedin U can influence eating behavior by promoting rejection of high-calorie foods and prefer more balanced diets.

The importance of decretins is derived from the study of Rubino, in which significant improvement was demonstrated in insulin secretion in undergoing surgical duodenal exclusion GK rats without impacting significantly on the secretion of GLP-1 but in the GIP.[34-36] However, in humans, it has been found that excluding a segment of foregut by EndoBarrier may favor weighted loss but does not result in significant differences going in terms of glycated HbA1c and fasting glucose. Similarly, with duodenal-jejunal derivation, complete remission of DM2 was demonstrated in only 10% of patients underwent the procedure,[37,38] which would support the fact that if there is a clinical effect, this is, marginal and could be due to other factors; so study suggests duodenal exclusion in the mouse model, in which a significative increase the concentration of GLP-1 improved insulin sensitivity, increased concentration of bile acids, and showed changes in microbiota at the expense of proteomics and bacteria firmicutes.[39]

In the other hand, ghrelin and galanin are two enterohormones that may favor the suppression of beta cells. The first is an orexigenic hormone secreted by the X/A cells in the antrum and the fundus may cause a reaction to fast to protect this induced hypoglycemia. The specific area where it acts is in the arcuate nucleus and the ventral tegmental area of the hypothalamus through the vagus afferents and direct secretion.[40] The enterohormone galanin, meanwhile, is expressed in neurons and intestine and suppresses the secretion of insulin-mediated glucose.

In the mouse model, there is evidence suggesting that diabetes favors increased to 100% by wet weight of intestine at the expense of hyperplasia in the proximal intestine, the site responsible for secretion decretins.

Considering this, the relationship between diabetes and intestinal length can be bidirectional. Individuals with higher intestinal length would exhibit impaired incretin by a late stimulus, which would tend to overfeed, hyperglycemia, and glucotoxicity against beta cells. Overfeeding favors intestinal hyperplasia, like DM, aggravating hyperglycemia by increasing the effect of decretins and decreased incretin effect.[41]

Similarly, ingestion of highly processed foods and "digestible," facilitate the absorption in the proximal intestine and secreted insulin; to be absorbed on this site, the distal stimulus would be less.

Bile acids

Bile acids are synthesized in the liver, steroids from the family of cholesterol, conjugated with taurine or glycine to increase hydrosolubility. There are two (classical and alternate) metabolic pathways initiated by seven alpha-hydroxylase and 27-hydroxylase, respectively. The classical pathway produces cholic acid and quenodeoxycholic acid, while the alternative pathway produces cholic acid mainly. Bile acids are secreted into the bile and excreted in reaction to food intake to aid digestion of fats.

In addition to the digestive functions of hepatobiliary secretions, bile acids possess endocrine effects and help in the regulation of glucose and lipid metabolism.[42]

Metabolic surgeries increase circulating concentrations of bile acids and activate the receptor FXR and TGR5. Being promoting the secretion of GLP-1 peptides and PYY.[43-45]

The FXR receptor is also expressed in beta cells and stimulates insulin secretion. Evidence and clinical based trials suggest that it had decreased hepatic gluconeogenesis and gluconeogenesis. Other activity was the mediated activation of FXR, secretion of fibroblast growth factor 19, the same that reduces the expression of seven alpha-hydroxylase inhibiting bile acid syntheses in the liver.

Interactions of bile acids are of primary importance in the secretion of GLP-1 as it was found in model animal

procedures (rats), which underwent duodenum-jejunal bypass, an interrupting of bile acid exposure to the epithelium. In addition, the duodenum-jejunum bypass favors a decrease in a proinflammatory state through the activation of JNK system in the liver and adipose tissue.[46] Hepatic steatosis improves due to the secretion of GLP-1, which is favored by the secretion of bile acids.

The TGR5 receptor is associated with proteinase G and expressed in adipose tissue, skeletal muscle cells, and L cells. Bile acids promote the secretion of GLP-1 through TGR5 in L cells.

It has been found that the biliary shunt of the terminal ileum promotes metabolic effects similar to those obtained after gastric bypass Roux by laparoscopy technique, including improvement of body weight, glucose tolerance, and hepatic steatosis. Furthermore, it has been found that the biliary bypass in the intestine, benefits from changes in the microbiota.[47,48]

Microbiota

Intestinal anatomy and dietary patterns model the microbiota, which has been associated with the pathogenesis of obesity, metabolic syndrome, diabetes, steatohepatitis, hepatitis, and other diseases.[49-51]

Firmicutes and Bacteroides dominate the bacterial population of the intestine of healthy humans, while in patients with obesity, decrease firmicutes, and metanobrevobacterias, which are able to extract more calories from the diet, increase and favoring failures in management.[52] The production of bacteria butyrates and propionates is associated with learning difficulties in patients with DM2.

By transferring the microbiota of patients undergoing surgery metabolic model in mice, it has been shown, that these contribute and improves the metabolic phenotype in rodents.[53] Both procedures, gastric bypass by Laparoscopic Roux as SG favor changes in the confirmation of the microbiota, increasing the number of Gammaproteobacteria, Bacteroides, Akkermansia, Verrucomicrobiales, and Escherichia; however, in the case of the second, these changes are temporary.[54]

Interactions between microbiota and human intestine are complex and apparently multilateral. In a study in mice on high-fat diets, they managed to identify exploratory, cognitive disorders and stereotypic behavior compared to those mice microbiota modeled by consuming control diet. Changes in the microbiota were evident diversities with alterations in the alpha and beta, in the other hand, taxonomically distribution associated with disruption markers of the intestinal membrane, increased expression in endotoxemia and TLR2, TLR4, and Iba1 by lymphocytes, which affects a greater state of neuroinflammation and impaired cerebrovascular homeostasis [Figure 1].[55-58]

PANCREATIC REGENERATION

Beta-cell failure is one of the characteristics common in advanced stages of DM2. The endoplasmic reticulum stress and oxidative stress are favorable to chronic depletion of beta cells and consequent dysfunction and death. It is proposed that glucotoxicity can silence genes of beta cells, such as those encoding Pdx1, Nkx6.1, MafA, and Pax6, promoting "dedifferentiation" to other cell lines (Ngn3+).[59] This event can be reversed by dietary changes, including fasting.

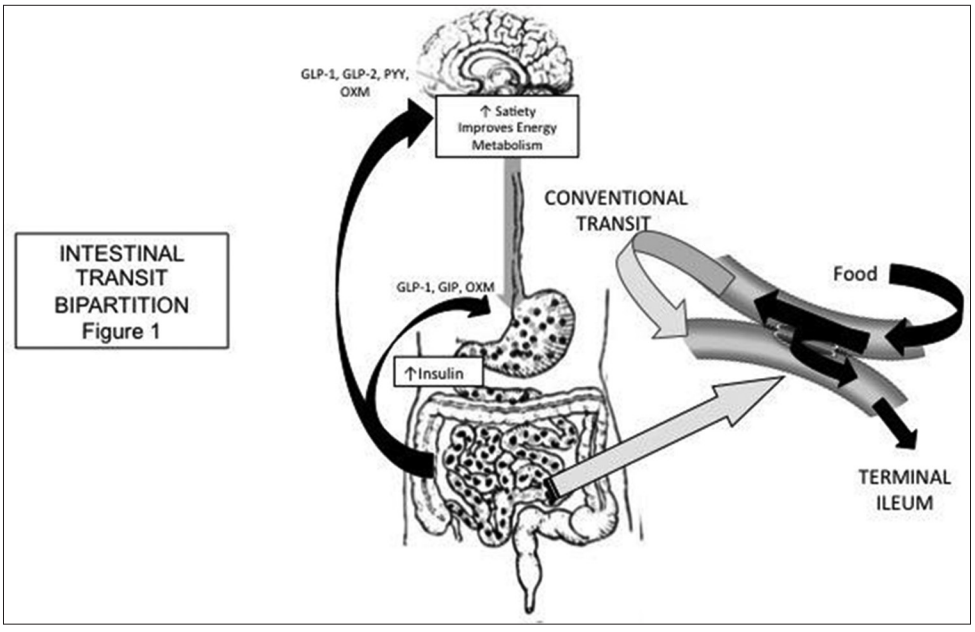

Figure 1: Neurohormonal axis, surgery of bipartition of intestinal transit

Until recently, it was considered that the beta cell mass was not able to resettle. However, there is evidence that the pancreatic regeneration action is possible through various mechanisms. The observed mechanisms are:

a) Inhibition of apoptosis and regeneration of the remaining beta cells.
b) Neogenesis from progenitor cells ductal.
c) Transdifferentiation cells, alpha, or beta cells to delta.

Among the effectors of this process are found glucagon and GLP-1 peptide.[60]

There are different mechanisms mediated by GLP-1 and other enterohormones, the increase in expression of gene products *REG* after anatomical modification. These products promote pancreatic regeneration, specifically, Reg3gamma, which has been associated with insulin concentrations and C-peptide in patients, who reacted favorably to gastric bypass Roux by Laparoscopy.[61-63]

Metabolic surgery, by increasing GLP-1 improves glycemic control even in patients with C-peptide negative, in which the absence of B cells is negative, regardless of etiology (DM2, DM1, and Latent autoimmune diabetes in adults). This suggests the existence of the clinical significant effect of this regeneration and gives greater importance to the activity of the products of metabolism of GLP-1.[64]

BIPARTITION OF INTESTINAL TRANSIT

The concept of intestinal transit bipartition has evolved from the need to stimulate incretin secretion by the distal intestine, without drying or exclude segments small intestine, as it happens in the adaptive enteromentectomy, gastric bypass Roux by Laparoscopy, biliopancreatic derivation, duodenum-jejunostomy, the duodenum-ileostomy anastomosis, etc.[65-67]

At present, bipartition of intestinal transit may be high or low. The high is represented by a gastroileostomy latero-terminal 180–250 cm proximal to the ileocecal valve with full-entero-side anastomosis to 80 cm proximal to the valve forming Y[68] forming omega[69] or by a duodenum-ileostomy latero-lateral.[70] The bipartition of the lower intestinal transit is achieved by a latero-lateral, jejunum-ileal anastomosis, calculated on a site agree with the total intestinal length of the patient, considering 1/3 jejunum and ileum 2/3, and the sum should not be <2.5 m or 33% of the total intestinal length.[71,72]

The following reason is that it is estimated that intestinal transit length of <200 cm of functional intestine can result in short bowel syndrome, as well as a minor segment of jejunum 35 cm (with jejunum-ileal anastomosis), <60 cm and lower jejunum anastomosis-colonic 150 cm with terminal jejunostomy.[73]

In other words, a patient with a jejunum-ileum 7 meters could be 100 cm anastomosis of Treitz and 200 cm from the ileocecal valve; thus, even with an exclusively transanastomotic step, the minimum length of 300 cm would transit, constituting 42.8% of the total length of the intestine, which prevents the possibility of short bowel syndrome.[74-77]

In a murine animal model, it was established that the most appropriate distance for derivation is between 50% and 60% of the total length of the jejunum-ileum, since, if less, there will be no effects on the regulation of glucose and, if greater, appear more often adverse effects like diarrhea.[78]

To promote a similar transit through the anastomosis, the length of this must be similar to the diameter of the intestinal loops. The following, to avoid complications such as demonstrated with non-ileal bypass jejunectomy described by Stockeld, 1991.[55] In this surgery, a latero-lateral 9 cm, 20 cm anastomosis of Treitz was made, with ileal located 25 cm from the ileocecal valve.[79-80] By making an anastomosis of at least twice diameter afferent loop, trans-anastomotic pressure favors preferential step, decreasing significantly in intestinal flow through the remaining intestine bacterial overgrowth, associated with malnutrition and hepatic disease, as reported at the time Stockeld [Figure 2].[55, 81-83]

The bipartition of intestinal transit is a modification of the intestinal bypass and reversible hypofunctioning of Lazzarotto e Souza. After calculating the intestinal absorption surface, using formulas given not validated, Lazzarotto e Souza underwent surgery 1200 patients, by jejunum-ileal anastomoses-side to side, considering not letting dysfunctionalize within 90 cm of the terminal ileum to avoid complications of nutritional nature. In his series, he reported a weight loss of 42.7% and complications such as diarrhea, nausea 9%, 0.6% anemia, hypoalbuminemia 0.83%, and extremely low rate of revision for a procedure that was used with bariatric purposes (0.24%).[84,85]

It was not until 10 years after the publication of Lazzarotto e Souza work that English speakers have reconsidered this type of surgery. Duan *et al.,*[57] bipartition, demonstrated that intestinal transit by latero-lateral anastomosis produces improvement in glucose homeostasis and the sensitivity to insulin and increase considerably concentrations of GLP-1 and total bile acids when compared to the model of the intestinal bypass and jejunostomy.[86,87] The jejunostomy is the main component in the entero-omentectomy adaptive proposed by Sergio Santoro, considerate as intestinal procedures favoring greater adaptation to environmental conditions rearrangements, enterohormones secretion by terminal ileum, as in humans was published in 2008 and

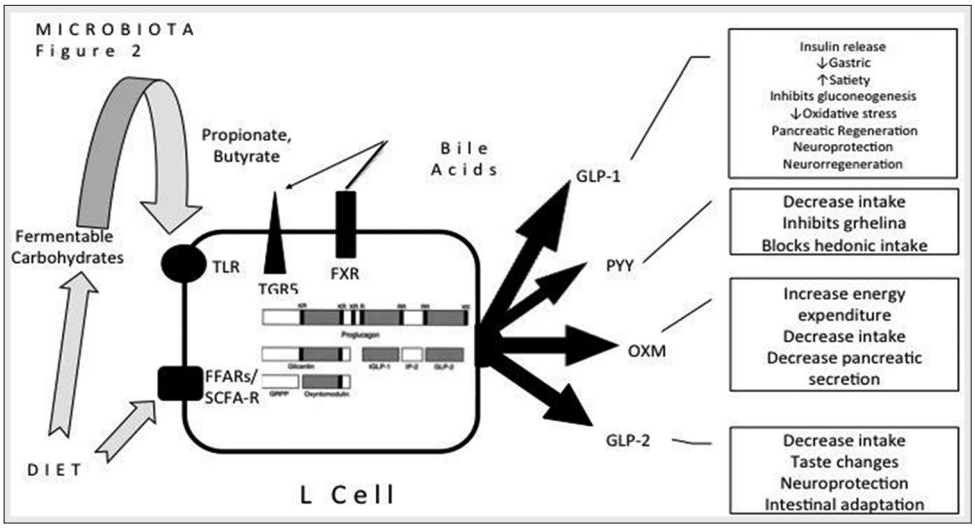

Figure 2: Microbiota in relation to diet and L. cells

reprinted in the murine model years later to reinforce the theory of the distal intestine stimulation.[88,89]

The enterohormone GLP-2 is secreted in an equimolar ratio with incretin GLP-1, and it functions is the inhibition of hunger, in hypothalamic arcuate nucleus level, in addition, reduction of hepatic glucose production and increase insulin sensitivity.[90]

A potential disadvantage with physical jejunostomy is known, that GLP-2 is one of the enterohormones associated with intestinal readaptative processes, and enteric to small bowel resection readaptation is related to magnitude of resection,[91-93] so a latero-lateral anastomosis could implicate less rehabilitation compared with jejunostomy if there were paracrine mechanisms that regulate activity of GLP-2.

The bipartition of intestinal transit could be made by conventional surgery, laparoscopic, or even totally endoscopic procedure assisted by magnets.

The partial derivation or bipartition jejunal intestinal transit jejunum-ileal assisted with magnets maintains the physiological principles of bipartition intestinal transit, and is achieved without the need for surgery.[94] However, between two major disadvantages. The first is the inability to close the mesenteric gap, exposing patients to the risk of complications from an internal hernia. The second difference lies in the open and laparoscopic procedures, in which the anastomosis is determined taking into account the complete intestinal length while, in the endoscopic procedure, ignore the length and, in addition, it is limited by the characteristics of the endoscope used, with the consequent risk of bacterial overgrowth, diarrhea, malabsorption, and other syndromes.

During the first study assisted by laparotomy, it was used with this endoscopic system, to identify the site of anastomosis 50–100 cm of Treitz and 50–100 cm from the ileocecal valve. Patients were able to made daily labors on the second day, on average activities. After 12 months they presented a loss of 40% of the excess weight (14.6% of total weight) and a 1.8% decrease of HbA1c (7.8+2.4%–59+0.5%).

Adverse effects in the first series of magnets operated patients, presented abdominal pain (90%), mild diarrhea (50%), and moderate (50%), Vitamin B (40%), and deficiency Vitamin D (20%), and iron (40%). However, changing intake habits, limiting carbohydrate intake, using loperamide or both resolved diarrhea.[95,96] At present, it is running the first randomized study to verify advantages or usefulness of the procedure (NTC03130244).

Previous experiences with bipartition of surgical intestinal transit suggest a reduction in HbA1c levels of over 2% in 53.3% patients, while 73.3% exhibit a greater decrease of 1.5%, and weight loss of about 12%. The functional parameters improved beta cells and concentrations of GLP-1. Complete remission rates of DM2 have been reported in 57–59%.[97,98]

By modifying the kinetics of incretins, GLP-1 and GLP-2 contribute to weight loss weight by their activity in gastric emptying and activation POMC system. The bipartition of intestinal transit might result in further loss of 10% of initial weight in 66.7% of patients.[99-101]

The metabolic effects include improvement in cardiovascular risk profile, reduced hypertension, and improved renal function parameters; however, it has also been documented decreased levels of Vitamin B12.

The most frequently reported side effects were diarrhea (46.7%), flatulence (26.7%), and pain (33.3%).

Bipartition of intestinal transit it does not produces blind loops. However, according to the length intestinal continuity, there may be deficiencies of micronutrients and macronutrients such as iron, zinc, Vitamin B, Vitamin D, calcium, and albumin. Another risk is dysbiosis, generating diarrhea with flatulence and bloating.[102]

In terms of safety, the procedure is clearly superior to other bariatric interventions that have complication rates of up to 10.5% and 0.5% lower mortality; furthermore, it is easily reversible.[103]

The remission of DM2 is achieved by surgical procedures, depending on the complex interactions between the microbiota, bile acids, and intestinal epithelia, rather than restrictive malabsorptive or restrictive. Bipartition of intestinal transit is a surgical option based on physiological principles responsible for remission of diabetes and is the easiest and safest for managing DM.[104,105]

CONCLUSIONS

In terms of safety, the procedure is clearly superior to other bariatric interventions that have complication rates of up to 10.5% and 0.5% lower mortality; furthermore, it is easily reversible.[103]

The remission of DM2 is achieved by surgical procedures, depending on the complex interactions between the microbiota, bile acids, and intestinal epithelia, rather than restrictive malabsorptive or restrictive. Bipartition of intestinal transit is a surgical option based on physiological principles responsible for remission of diabetes and is the easiest and safest for managing DM.[104,105]

CONFLICTS OF INTEREST

None.

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