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USE OF LIRAGLUTIDE FOR WEIGHT LOSS IN OBESE OR OVERWEIGHT PATIENTS ASSOCIATED WITH COMORBIDITIES: A LITERATURE REVIEW

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Abstract: INTRODUCTION: Obesity and overweight are hotly debated topics, as they are risk factors for several diseases and their current treatment and prevention are inefficient. In this sense, Liraglutide, initially used to treat type 2 diabetes mellitus, is now being investigated with a view to weight loss. **OBJECTIVE:** To review the action and effectiveness of using Liraglutide in non-diabetic patients for weight loss, comparing it with other treatments for the same purpose, in different studies. **METHODS:** Integrative literary review of articles from the PubMed and Lilacs databases, using as keywords the terms "Liraglutide", "Weight Loss", "Obesity" and "Diabetes Mellitus" published between 2016 and 2021. **RESULTS:** Among the 11 articles used, it was observed that Liraglutide can promote increased satiety and can cause changes in the gastrointestinal tract, consequently causing a reduction in food intake and loss of body weight. However, it also raised concerns related to several factors and adverse reactions resulting from its use. **CONCLUSION:** Liraglutide has been shown to be effective for weight loss in non-diabetic patients, especially when combined with dietary re-education and behavioral therapy. However, as it is a relatively new medication, attention must be paid to possible adverse reactions.

Keywords: Liraglutide; Obesity; Weight loss; Diabetes Mellitus;

INTRODUCTION

The Brazilian Society of Endocrinology and Metabolism defines obesity as the excessive accumulation of body fat, where the body mass index presented is greater than 30[1]. Obesity and weight gain are extremely complex and multifactorial conditions, which involve, for example, environmental and genetic factors.[2]

It is known that current treatment and prevention, in epidemiological terms, are

still inefficient: in Brazil, obesity increased from 11.8% in 2006 to 19.8% in 2018 and it is estimated that, By 2025, 2.3 billion adults around the world will be overweight[3]. Among the reasons that make such data worrying for public health is the fact that overweight and obesity are risk factors for several diseases.[2] Furthermore, such conditions can also cause economic, psychological and social losses, which which also justifies greater attention from the scientific community to the search for more effective treatments.[4]

Among the treatments available today, we can mention those that use medication and those that do not, as well as treatment with gastroplasty surgery. Non-drug treatments include: behavioral therapies, changing eating habits and practicing physical exercise. Among the medications used for weight loss are, for example: catecholaminergic, serotonergic, thermogenic drugs, and selective CB-1 antagonists, many of which have been monitored for efficacy and safety. [4] There are also, the possibility of a non-drug treatment being associated with the use of drugs and/or surgical treatment.

In addition to the aforementioned drug classes, in recent years, antidiabetics have also been studied for the same purpose, with liraglutide being one of the promising representatives of the category.

Therefore, liraglutide is a medication analogous to the GLP-1 incretin hormone, that is, it participates in the control of glycemia by increasing the release of insulin[5-7] and reducing the secretion of glucagon[5,6]. Its mechanism of action is the activation of GLP-1 receptors, belonging to the family of receptors coupled to G proteins, found in the plasma membrane of pancreatic beta cells, cells of the heart, kidneys, lungs, and central nervous system.[5,8]

GLP-1 is released by L cells of the intestinal mucosa after food intake, in response to the presence of nutrients[8], and its effects on plasma glucose levels have led to the therapeutic potential of this hormone being investigated. However, the low half-life of GLP-1, due to its degradation by the enzyme dipeptidyl peptidase-IV (DPP-IV)[9-11], indicated a limitation in the medicinal use[5,8] of this component and generated a demand for GLP-1 analogues that had a longer half-life.

From this perspective, initially as a treatment for type 2 diabetes mellitus, liraglutide, a long-acting GLP-1 receptor agonist, which is structurally 97% homologous to human GLP-1, but contains an amino acid substitution and the introduction of a fatty acid chain, which increases the stability of the molecule, guaranteeing a half-life of between 10h-14h[8]. The fatty acid in liraglutide allows its reversible bond with albumin, which increases the molecule's protection against the degradation of DPP-IV[5,8], decreases its renal filtration5 and its absorption rate[8].

Thus, there now exists a GLP-1 analogue capable of maintaining high and stable plasma levels, an essential characteristic for the possibility of its effective pharmaceutical use[12].

Subsequently, the effects of GLP-1 and its analogues on decreased food intake, feelings of satiety and weight loss[5,8] began to be investigated, aiming at the possibility of using this medication for the treatment of overweight and obesity. The mechanisms of action of liraglutide on food intake and weight loss have not yet been completely elucidated, however, studies indicate that it has peripheral and central action on the nervous system[8], unlike GLP-1, which appears to act in a significant, only on peripheral GLP-1 receptors[13]. Thus, the most current hypotheses suggest that liraglutide acts on areas of the central nervous system that participate in the control of hunger and satiety, delaying gastric

emptying and on reward and motivation areas of the brain, having an effect not only on intake, but also changing food preferences and improving individuals' metabolic rates[8].

Thus, despite the therapeutic potential of liraglutide, caution is needed when prescribing it, as it is a new drug, all safety data is not yet available, and concerns related to various factors and adverse reactions resulting from its use are necessary. [14]

OBJECTIVES

To review the action and effectiveness of using liraglutide in non-diabetic patients for weight loss, comparing it with other treatments for the same purpose, in different studies.

METHOD

Through the DeCS website (www.decs.bvs.br), the descriptors "Liraglutida", "Perda de Peso", "Obesidade" and "Diabetes Mellitus" were selected and their respective translations into English were also carried out by DeCs: "Liraglutide", "Weight Loss", "Obesity" and "Diabetes Mellitus". Such descriptors were combined to create search strategies, searching for the presence of such terms in the title and abstract, as follows:

A) Liraglutide AND Obesity NOT Diabetes Mellitus;

B) Liraglutide AND Weight Loss NOT Diabetes Mellitus;

The 2 aforementioned arrangements were used in Portuguese and English in searches in the PubMed and Lilacs databases, with the following filters also being applied: human, clinical trials and randomized clinical trials. As an inclusion criterion, only articles published between 2016 and 2021 were also selected. All abstracts found were read and were excluded from the search: articles that included diabetics in the methodology, specific articles about children and adolescents and articles that explicitly evaluated populations with other comorbidities associated with obesity and overweight.

RESULTS

After analyzing the selected articles, the most prominent information found in the theoretical references is available in Table 1 and will be explored in the "Discussion" topic.

DISCUSSION

The effectiveness of using liraglutide for weight loss compared to the use of placebo can be demonstrated by analyzing the comparison made by Halawi et al. (2017) Halawi et al. (2019), M Farr et al. (2019), Tronieri et al. (2020) and Ludgren et al. (2021).

Halawi and colleagues (2017) conducted a randomized pilot study that compared the effects of liraglutide versus placebo on gastric motor functions, satiety, and weight fluctuations in obese individuals over sixteen weeks. The weight loss effects of liraglutide were associated with delayed gastric emptying of solids in the fifth and sixteenth weeks, and studies showed that delayed gastric emptying in the fifth week correlated with increased weight loss with liraglutide in four months, suggesting that gastric emptying may be an important biomarker to determine the feasibility of prolonged treatment with this medication.[16]

Thus, compared to placebo, the use of liraglutide provided a delay in the gastric emptying of solids, and significantly reduced the weight of the individuals.[16] In the sixteenth week, the rate of gastric emptying in participants treated with liraglutide increased significantly by compared to the fifth week, although these participants still had slower gastric emptying that week than the placebo group. Other studies have suggested that the tachyphylaxis of the gastric emptying response has been hypothesized to reflect

Author no	Title	Kind of study	Goals	Results
O'Neil et al. (2018) 14	Efficacy and safety of semaglutide compared with liraglutide and placebo for weight loss in patients with obesity: a randomized, double-blind, placebo and active controlled, dose-ranging, phase 2 trial	Rehearsal clinical randomized on=957	Assess effectiveness and security of GLP-1 in comparison to liraglutide and placebo in promotion of weight loss.	Weight loss for the group placebo was around -2·3% versus -6·0% (0·05 mg), -8·6% (0·1 mg), -11·6% (0·2 mg), - 11·2% (0·3 mg), and -13·8% (0·4 mg) for semaglutide groups. In compared to liraglutide, the results were -13·8% until -11·2% (semaglutide) vs -7·8% (liraglutide).
Wadden et. al. (2018) 15	Intensive Behavioral Therapy for Obesity Combined with Liraglutide 3.0 mg: A Randomized Controlled Trial	Clinical trial randomized n=150	Compare the loss weight in obese people exclusively with therapy behavioral versus with therapy behavioral and use of liraglutide	44.0% (therapy only behavioral), 70.0% (therapy behavioral and liraglutide), and 74.0% (behavioral therapy, liraglutide and diets of 1,000 to 1,200 kcal/d) of participants lost ≥ 5% of body weight. The loss of weight in all groups was associated with a significant reduction of risk factors cardiometabolic.
Halawi et al. (2017) 16	Effects of liraglutide on weight, satiation, and gastric functions in obesity: a randomized, placebo-controlled pilot trial	Pilot study randomized n=40	Compare the effects of liraglutide versus placebo in motor functions gastric pressure, satiety and weight	Compared to placebo, the liraglutide delayed emptying gastric solids, observed in week 5, (median 70 min [IQR* 32 to 151] vs 4 min [-21 to 18]; p<0·0001) and at week 16 (30·5 min [-11 to 54] vs -1 min [-19 to
			in individuals obese per 16 weeks.	7]; p=0·025). There was also significant greater loss of weight in the group using liraglutide compared to the group placebo (at week 5: median 3·7 kg [IQR 2·8 to 4·8] vs. 0·6 kg [-0·3 to 1·4], p<0·0001; in week 16: 5·3 kg [5·2 to 6·8] vs 2·5 kg [0·1 to 4·2], p=0·0009). The feeling of satiety during nutrition was assessed by maximum tolerated volume, measured at week 16, and was lower in the liraglutide group (median 750 mL [IQR 651 up to 908]) compared with the placebo group (1126 mL [944- 1185]; p=0·054). They were not observed differences significant between groups regarding the feeling of satiety after eating, filling volume or fasting gastric volumes and postprandial at week 16.
Halawi et al. (2019)17	GLP-1 Analog Modulates Appetite, Taste Preference, Gut Hormones, and Regional Body Fat Stores in Adults with Obesity	Study clinical randomized controlled n=35	Compare with placebo effects of liraglutide in appetite, preferences food, local deposition of fat body and measures anthropometric	Compared to the group placebo, the liraglutide group had significant reductions in maximum tolerated volume, in potential consumption score of food, in the desire to eat something sweet/ salty/tasty/fatty o, and an increase in perception of satiety. LPG levels- 1 decreased and PYY levels increased in plasma after prandial in the group using liraglutide. Significant reductions in fat were observed without reduction in body mass slim.
M Farr et al. (2019)18	Longer-term liraglutide administration at the highest dose approved for obesity increases reward- related orbitofrontal cortex activation in response to food cues: implications for plateauing weight loss in response to anti-obesity therapies	Study clinical randomized n=20	Understand the actions of using long term of maximum dose of liraglutide for weight loss in frames obesity in nervous system central	While using liraglutide, patients lost more weight, had a reduction in fasting blood glucose (P <.001) and showed improvement in levels of cholesterol. The activation brain in response to images of food were not altered by liraglutide vs. placebo. Liraglutide increased activation of the cortex right orbitofrontal in response to signs of food (P < .016, related to multiple comparisons).

M Floor et al. (2019)19	Changes in health-related quality of life with intensive behavioral therapy combined with liraglutide 3.0 mg per day	Rehearsal clinical randomized on=150	Examine the effects of therapy behavioral intensive (IBT) for treatment of obesity, associated or not liraglutide and controlled diet in changes general in condition of health, in quality of life and weight.	The groups treated with liraglutide achieved improvements related to total weight and better quality of life clinically significant that the group that used only IBT. The groups using liraglutide also achieved greater improvements related to weight-related distress and in mental health, measured by SF-36 score. Regardless of the group, the weight loss has been associated with greater improvements in quality of life (general and weight-related).
Capristo et al. (2018)20	Intensive lifestyle modifications with or without liraglutide 3mg vs. sleeve gastrectomy: A three-arm non-randomized, controlled, pilot study	Rehearsal clinical (n=75)	Compare the effects of intense lifestyle modification (ILM) associated or not with liraglutide with the effects of gastrectomy vertical (sleeve) about the BMI of patients.	Sleeve gastrectomy (SG) reduced BMI by32% (P<0.001 vs. clinical intervention), while ILM-liraglutide and ILM alone reduced24% and 14%, respectively (P<0.001). A average weight loss was- 11.6kg with SG, -8.3kg with ILM-liraglutide and -6.3kg with isolated ILM.
Iepsen et al. (2018)21	Patients with Obesity Caused by Melanocortin-4 Receptor Mutations Can Be Treated with a Glucagon- like Peptide-1 Receptor Agonist	Rehearsal clinical (n=42)	Compare to efficiency of liraglutide in treatment of patients with obesity monogenic, caused by mutation in receiver of melanocortin- 4 (MC4R), as treatment of patients obese without mutation.	Liraglutide treatment (3 mg/day) for 16 weeks took to a weight loss of6.8kg ± 1.8kgin the group with MC4R mutation and6.1 kg ± 1.2 kg in the group without mutation, whatdemonstrated significant clinical equivalence between the two groups, promoting a loss of weight of approximately 6%.
Tronieri et al. (2019)22	Effects of Liraglutide on Appetite, Food Worry, and Food Liking: Results of a Randomized Controlled Trial	Rehearsal clinical randomized the controlled (n=113)	Compare the long-term effects deadline in changes of appetite in patients obese treated with intense therapy	In the 52nd week the average groups weight loss treated exclusively by IBT, per IBT-liraglutide and multicomponent were, respectively,6.2kg ± 1.6%, 11.8 ± 1.6% and 12.1 ± 1.5%. In the 6th week, compared to members
			behavioral (exclusive IBT), with IBT associated with liraglutide (IBT-liraglutide) and with IBT, liraglutide and diet (multicomponent It is) .	of the exclusive IBT group, the patients in the IBT group- liraglutide reported higher hunger reductions (-0.3 ± 4.2 vs. -16.8 ± 4.0 mm, p = .005), preoccupation with food (+0.2 ± 3.7 vs -16.3 ± 3.6 mm, p = .002) and increased satiety (- 5.1 ± 3.2 vs +9.8 ± 3.0 mm, p = .001), the which continued until the week 24. They were also observed, until the 24th week, differences significant in reducing the hunger and concern about group food multicomponent, when compared to exclusive IBT.
Tronieri et al. (2020)23	Effects of Dietary Self-Monitoring, Physical Activity, Liraglutide 3.0 mg, and Placebo on Weight Loss in the SCALE IBT Trial	Rehearsal clinical randomized the double blind (n=282)	Evaluate the contributions from adherence to medicine, the self- monitoring food and recommendations of activity physics for weight loss in patients obese receiving intense therapy behavioral (IBT).	Compared to non-adherence, full membership to self- food monitoring and activity recommendations physics had, respectively, estimated weight change of- 7.2% (95% CI -10.4 to -4.0; p < 0.0001) and -2.0% (95% CI -3.2 to -0.8; p = 0.0009). A complete adherence to liraglutide, compared to non-adhesion of the medication, presented a additional weight loss estimated -6.5% (95% CI - 10.2 to -2.9; p = 0.0005), while The non-adherence to placebo presented It is made significant in the loss of weight (p=0.33).
Ludgren et al. (2021)24	Healthy Weight Loss Maintenance with Exercise, Liraglutide, or Both Combined	Rehearsal clinical randomized the controlled (n=195)	Assess the effects of the use of liraglutide associated or not the activity vigorous physical about the	All interventions generated greater weight loss than placebo: placebo with activity vigorous-4.1 kg (95% confidence interval [CI], -7.8 to -0.4; P = 0.03); liraglutide with usual activity, -6.8 kg (95%

			changes of body weight, percentage of body fat and changes metabolic. A security of interventions It was also evaluated.	CI, -10.4 to -3.1; P<0.001); liraglutide with vigorous activity, -9.5 kg (95% CI, -13.1 to -5.9; P<0.001). Liraglutide associated with physical activity vigorously led to a loss of weight greater than that of the activity vigorous physical with the placebo, but not than liraglutide with usual activity. However, with regard to the decrease in the percentage of fat, the combined strategy was more efficient than isolated interventions.

Table 1: Most prominent information found in theoretical references

*IQR: Interquartile range

continued activation of GLP-1 receptors by these agonists, leading to possible tolerance.[16, 22] This mechanism may reduce the effect of GLP-1 agonists, such as liraglutide, on the perception of hunger and satiety, so that participants no longer experience noticeable appetite control after twenty-four weeks of treatment, at which point weight loss typically begins to slow or reach a plateau.[16] In this context, we can also observe that anorexigenic hormones, such as leptin, decrease and orexigenic hormones, such as ghrelin, increase after weight loss, which can contribute to a greater perception of hunger. Obesogenic social and environmental factors, such as an abundance of highly palatable foods, may also "wear out" the neural effects of liraglutide on reward pathways and may increase the desire to consume food. With this in mind, the combination of medication and physical activity is important to mitigate this effect. [16]

A new randomized controlled clinical study was carried out by Halawi and colleagues (2019), with the aim of comparing the effects of liraglutide on appetite, taste preference, regional body fat deposits and anthropometric measurements with placebo.[17] Thirty participants participated in the study. and five individuals, with the group that used liraglutide having a greater feeling of satiety and a significant decrease in the desire to eat sweet, salty and tasty foods.[17] It was then found that liraglutide can lead to weight loss, partly due to changing taste preferences. A decrease in GLP-1 levels was also observed, and an increase in PYY in relation to the basal value.[17] These hormones participate in the speed of gastric emptying, acid secretion, decrease the speed of intestinal transit, activate greater production and insulin secretion and, simultaneously, deactivate anti-insulin hormones, cause a rapid removal of fats from the blood and finally, cause an intense sensation of satiety upon reaching the central nervous system. Therefore, these peptides not only control the amount of food ingested, but also participate in food choices and preferences. Therefore, it is conceivable that future classes of compounds that target the receptors of these peptides could impact eating behavior, thus inducing a preference or aversion to certain types of foods, acting in addition to their effects. At the end of the study, significant reductions were observed in the body as a whole, trunk and upper and lower body fat, without a reduction in lean body mass.[17]

M. Farr and collaborators (2019) promoted a randomized clinical study to understand how the action of liraglutide works in the long term and at high doses.[18] This study was carried out in obese people and with central nervous system disorders related to hunger and satiety. It was shown that patients who used liraglutide showed an improvement in glycemic and lipid levels, in addition to reports of reduced food intake. What was seen in the first analysis of the study is that there was no change in brain activation, but, within five weeks, patients had significant weight loss,

and once weight was controlled, an increase in brain activation was observed. frontal orbital cortex related to reward for highly palatable foods.[16, 17] Therefore, the authors highlight that the effects on brain activation were in the opposite direction to those observed in short-term studies.

In this sense, it is believed that this is a counter-regulatory mechanism, in which weight loss causes early increases in right orbitofrontal cortex activations for food cues, leading to the eventual weight loss plateau. These data point to a promising focus for additional interventions that, by contributing to the CNS reward system, could provide tangible benefits in reversing the plateau phenomenon and promoting greater weight loss.[17]

Recently, a 2021 clinical study by Ludgren and colleagues promoted a randomized controlled clinical study, with the aim of investigating the best approaches to maintaining lost weight through long-term dietary strategies using exercise, diet and medication. The use of liraglutide in association with a varied physical exercise program and a low-calorie diet was compared. After an eight-week low-calorie diet, one hundred and ninety-five participants had an average reduction in body weight of 13.1 kg. Within one year, all active treatment strategies led to greater weight loss.[24] The "exercise alone" and "liraglutide alone" groups led to the maintenance of initial weight loss, with a reduction in fat mass. It is known that losses of 5% to 15% of initial body weight are achievable in most high BMI groups with moderate to low calorie dietary strategies and behavioral approaches, at least in the short term. It is the long-term maintenance of this weight loss that has been difficult for most patients struggling with obesity. This occurs because, after weight loss, rapid weight gain may occur due to hormonal changes in appetite control, which favor weight gain, in addition to lower total energy expenditure.[24]

This study supports the fact that the additive effect of healthy lifestyle patterns and a medication that helps with body weight adjustment is a good choice to achieve weight maintenance and a healthier metabolic profile, therefore there is no treatment pharmacological treatment that does not involve a change in lifestyle, as this factor enhances positive results.

Therefore, it is fundamentally important to develop a multidisciplinary program of continuous actions that allow the identification, control, prevention and, above all, education of the factors that predispose to obesity.[23, 24.,]

Among the possible existing non-surgical interventions for weight loss, in addition to medication, lifestyle modification, through the adoption of physical activities, diets and psychological support has demonstrated positive results in the treatment of obese individuals.[15]

One of the approaches therapies that have shown good prognoses is the technique known as Intensive Behavioral Therapy (IBT), which consists of identifying and changing dysfunctional behaviors that make it difficult to lose and maintain weight and quality of life of these individuals.[25] In this context, several studies sought to understand the effects of the association between these two interventions through the use of liraglutide combined with IBT sessions. The first to propose this relationship was Wadden and collaborators in 2018, in a randomized clinical trial with the participation of 150 people and conducted by 52 weeks, which aimed to evaluate the differences between a treatment based solely on Intensive Behavioral Therapy and its combination with the medication liraglutide and an appropriate diet. Through the results, a positive statistical difference was observed in

the effect of the combination of these elements, that is, the proportion of participants in the group exposed to both psychotherapeutic management and medication who presented a weight loss greater than or equal to 5% of their weight. body weight was greater than that of the group exposed only to therapy. The same scenario was observed in individuals who, in addition to these two measures, also adopted a controlled diet of 1000–1200 kcal/day, achieving even more significant results. It is important to point out that in all three interventions, weight loss was associated with a significant reduction in cardiometabolic risk factors.[15]

In addition to clinical issues related to obesity and overweight, another important aspect to be analyzed is the individual's quality of life. This assessment takes into account how the patient perceives their physical, mental, emotional and social state. There are several factors that can negatively influence this perception, including body weight.[19] In view of this context, M Chao, et al. in 2019 used the same methodological components used by Wadden et al. (2018) in their study, in which the effectiveness of using liraglutide associated with IBT in weight reduction was identified [15], in order to obtain data regarding the effects of this same association on the general quality of life related to health and weight reported by the patient. To reach these results, standardized international questionnaires were used, such as the "Short Form-36 Health Survey" (SF-36) and the "Impact of Weight on Quality of Life-Lite" (IWQOL-Lite), which cover different domains of life. [19] Taking into account the fact that the same eligibility criteria and the same protocol were used to conduct the treatment, as observed by Wadden and collaborators in 2018, M Chao et al. (2019) found similar results at the end of the 52º week of the experiment, with weight loss in the two groups treated with liraglutide being significantly greater than in the group treated exclusively with IBT sessions. Based on this difference, it was possible to evaluate how changes in body weight influence the quality of life reported by the individual, and based on the report generated after the application of the questionnaires, it was noted that there was a more significant improvement in the values attributed to quality of life. life both related to health and weight obtained in the groups treated with liraglutide, which had also already presented better results in relation to total weight, when compared to the scores expressed by the control group, which also presented lower weight loss values.[19]

It is believed that the additional benefits generated from the association between behavioral and pharmacological treatments are related to the complementarity of their mechanisms of action.[26] There are indications that liraglutide has both peripheral and central action in the nervous system, acting on areas that make up the control of hunger and satiety.[26] In previous studies such as those proposed by Wadden et al. (2018) and M Chao et al. (2019) there was consensus regarding the effectiveness of this medicinal addition in increasing weight loss and promoting positive effects involving appetite management. However, how these changes occur and how long they persist has not been completely elucidated.[22] In the randomized clinical trial carried out by Tronieri and colleagues in 2019, it was found that the addition of liraglutide to Intensive Behavioral Therapy treatment indicated greater reductions in hunger. and preoccupation with food, in addition to an increase in satiety from the sixth week of the experiment lasting until the 24º, from which no significant differences were noted until the 52° week.[22] This same effect, which is called Tachyphylaxis, was cited by Halawi et al. (2017), when evaluating the influence of liraglutide on gastric emptying.[16]

In this context, it is common that participants have the feeling that the medication is no longer performing its function, since their perceptions regarding their hunger control are reduced, however, when analyzing the results regarding final weight loss, the effectiveness is noted of combination.[16, 22] Tronieri, et al. (2020) estimated that complete adherence to the administration of liraglutide, that is, the use of 3.0 mg of the drug at least once a week, throughout the 56 weeks of the experiment, promotes an additional weight loss of around 6.5%, which when compared to non-adherence values, represents a considerable improvement.[23] The influence of adherence to the diet and recommendations for physical exercise practices was also evaluated, with adequate nutrition carried out on a constant basis having a greater impact in the final result than performing physical activity. All of these components were analyzed considering their common basis, treatment with Intensive Behavioral Therapy.[23]

Pointing out a specific cause for excess weight is a complex attribution, especially when taking into account the fact that common obesity, also known as polygenic, is due to a multifactorial process, based on a set of small changes, which act on various metabolic pathways, however, knowing the systems involved in this situation allows the development of more objective and more targeted therapies.[27] In this context, it is important to recognize the influence of genetic inheritance on the predisposition to obesity, especially those generated by monogenic forms, which they result from the mutation or deficiency of a single gene.[27] The use of liraglutide was evaluated by Iepsen et al. (2018) as a possible therapeutic resource for the most common cause of monogenic obesity, mutation in the melanocortin-4 receptor (MC4R). The results obtained in the experiment demonstrate that regardless of whether the MC4R pathway is preserved or not, the effects on appetite control of liraglutide were observed in both groups, thus favoring clinically significant weight loss in both mutated individuals and those without. the mutation, this similarity can be interpreted as a good indication for the application of this drug in the treatment of this condition. [21]

Successful clinical trials demonstrating the applicability of liraglutide have led to increased interest in therapies based on GLP-1 analogues, including semaglutide.[14] Although they have the same mechanism of action, but have different administration intervals and doses, semaglutide, for example, allows a single weekly application with a dosage of 2.4 mg, while liraglutide requires daily doses of 3.0 mg. This difference represents a functional advantage, as it frees the patient from the discomfort generated by constant needling, allowing this process to be limited to a single day of the week.[14] The use of semaglutide for weight control in adults with obesity was approved by the Food and Drug Administration, the federal agency of the United States Department of Health and Human Services, in first half of 2021.[28] This permission was based on previous studies such as the one carried out by O'Neil et al. (2018) who sought to evaluate the efficacy and safety of this drug by comparing it to placebo and liraglutide, a medication already approved and in widespread use.[14] The findings of the clinical trial show greater effectiveness in the application of semaglutide when compared to liraglutide, presenting more pronounced weight loss. Despite being promising, little is known about its long-term effects, as is the case with liraglutide, making it necessary to monitor the repercussions of its use over time.[5,14]

Surgical treatment has also been shown to be an effective intervention in the clinical management of some cases of obesity, it can

be indicated for patients with BMI ≥ 40 kg/m² or those with BMI ≥ 35 associated with comorbidities such as: cardiovascular risk, difficult-to-control diabetes mellitus, sleep apnea syndrome and degenerative joint disease.[29]

Although it is a safe technique with low mortality rates, adherence to this treatment modality is reduced, as surgery is seen as a risky procedure.[20] In this context, the evaluation of the effectiveness of gastrectomy when compared to the use of medications combined with Changes in lifestyle are an important point for analyzing the risk-benefit relationship of this strategy. Capristo et al. (2018) found that the daily injection of liraglutide at a dose of 3.0 mg associated with a regulated diet and physical exercise promoted significant weight loss, however this value was 25% lower than that found in the group undergoing sleeve gastrectomy.[20] Therefore, despite the surgical approach presenting better overall results, the risks and complications involved in this process are still significant for specific groups of patients, so that an individual analysis of the applicability of this method and the consideration of other treatment programs are necessary. weight loss that would also achieve a satisfactory outcome.[20]

CONCLUSION

The substance liraglutide is a medicine approved by ANVISA for sale in Brazil since March 2010, with the purpose of specific use in the treatment of type 2 diabetes mellitus. But it was only in 2016 that Anvisa approved the registration of the medicine Saxenda (liraglutide) for chronic control of weight, in association with a low-calorie diet and increased physical exercise.[30]

After an analysis of the effectiveness of liraglutide for the treatment of people with obesity and overweight associated with comorbidities, it was possible to conclude that the medication is effective, especially when used concomitantly with dietary re-education, physical exercise and behavioral therapy, with the weight loss action of liraglutide a combination of effects on the CNS and GIT.

However, as it is a relatively new medication, where information about its safety and effectiveness has recently arrived on the market, it is therefore necessary to carry out other, more robust analyzes on side effects, and dosages in larger samples, so that it can be It is possible to better parametrically see the advantages and disadvantages of using this drug for the treatment of obesity.

From the damages presented and analyzed, it was possible to understand that the treatment of obesity is complex and multidisciplinary and that it is therefore necessary to always be aware of new therapies for its prevention and treatment. In general terms, pharmacological treatment is an adjunct to targeted therapies focused on modifying lifestyle habits related to nutritional guidelines to reduce calorie consumption in food and exercise to increase calorie expenditure. Everything must be individualized, under ongoing medical supervision and maintained when safe. Like any chronic disease, pharmacological treatment begins with secondary prevention to prevent the disease from progressing to a more serious stage and prevent complications. There is no long-term pharmacological treatment that does not involve lifestyle changes.

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