

THE RELATIONSHIP OF GUT MICROBIOTA AND OBESITY AND TREATMENT WITH SEMAGLUTIDE

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Abstract: This article seeks to address obesity as a highly prevalent pathology, which causes a high degree of morbidity and mortality due to its complications and the illnesses that result from it. In this sense, the use of semaglutide and similar products is discussed, given that the Federal Drug Administration (FDA) and Anvisa have already admitted the registration of the aforementioned medication for weight control in adults, under medical indication, and the guidance for its use is always accompanied by a low-calorie diet and physical exercise. The release of this, as an adjuvant medication in the treatment of obesity, has its action on the intestinal microbiota, thus presenting its effectiveness and the relationship between the specific action of the medication and the results presented. The present study used a literary review that will seek to be based on scientific articles and other publications related to the topic covered. The sources will be accessed in recognized databases, such as Google Scholar and the Scielo Databases. To this end, publications from the last 10 years will be selected. As results of this study, the interaction between the intestinal microbiota and intrinsic obesity can be observed, and treatment with semaglutide has shown promising potential not only for weight loss, but above all for the modulation of the microbiota, bringing an integrated approach to treatment. of obesity.

Keywords: Obesity. Semaglutide. Treatment. Intestinal microbiota.

INTRODUCTION

The number of obese people has increased significantly, mainly due to factors that can be treated and capable of being modified, including inadequate diet and a sedentary lifestyle. This disease is gaining notoriety, because in addition to the growing number of people who develop it, the consequences of this untreated disease go far beyond the aesthetic issue, causing a significant loss of quality of life and significant morbidity in many cases (BUCHEIT et. al., 2020).

There is important research being carried out to prove the attribution of the composition of the intestinal microbiota to environmental factors and weight control. The human intestinal microbiota is made up of approximately 100 trillion bacteria, with more than a thousand distinct species. The intestinal microbiota cooperates with metabolism and works to convert food into nutrients and consequently into energy (VILARRASA et. al., 2023).

In the Brazilian pharmaceutical market there are few medicines approved by the responsible bodies to treat obesity. The release of liraglutide in 2017 was widely celebrated by patients and healthcare professionals, and later semaglutide, which gained market share due to its more simplified mode of action. (CAPRISTO et. al., 2017)

This work is justified by the fact that obesity is an important disease and the number of medicines allowed for consumption for its treatment is quite restricted, this way, for each new drug released for commercialization and which has undergone efficacy and Safety is a reason for expectation and attention among patients and professionals in the field. The problem to be answered in this study is: How does semaglutide contribute to reducing obesity and improving metabolic parameters in obese patients?

The general objective of this study is to discuss the action of the drug semaglutide in

the treatment of obesity and the relationship between the intestinal microbiota and this disease. As specific objectives, we will seek to address general considerations about obesity; relate the intestinal microbiota with obesity, in order to understand the action of medications in this part of the body; describe semaglutide in its composition, indications, contraindications, dosage, side effects and adverse reactions and its action in the treatment of obesity.

In this sense, we discuss the use of a drug to treat obesity, as a relevant factor within the contemporary context, given the reality of the increase in the number of patients with obesity and difficulty losing weight alone, considering the direct action of the intestinal microbiota. in the weight loss process must be considered (BUCHEIT et. al., 2020).

METHODOLOGY

This study is a narrative review, where data collection was used, through bibliographic research in the following electronic libraries: SciElo, Medline and Pubmed, selecting scientific publications from the last 10 years, these being the inclusion criteria, as well as the exclusion criteria cover extra-temporal publications or those that did not cover the defined theme. Among national and foreign publications, 10 articles were selected that met the search criteria. The following descriptors were used for the research: obesity, drugs for obesity, intestinal microbiota and semaglutide.

Despite the limitation of more recent materials on the subject, scientific input was provided for the construction of this project, distinguishing the basic concepts about the disease, as well as the pharmaceutical approach and the new medications being studied to treat it. Bibliographic and documentary research, with the technique of indirect documentation, will be used through readings in articles and technical-specific publications, and other works that address the subject discussed.

DEVELOPMENT

Obesity is a pathology that arises from a complex mix of genetic, environmental and metabolic factors, in addition to being influenced by cultural, behavioral and even psychological issues, which over time cause an imbalance in the body, resulting in emergence of other interrelated illnesses. This occurs because obesity is intrinsically linked to several chronic diseases, such as systemic arterial hypertension, type 2 diabetes mellitus, cardiovascular diseases, dyslipidemia, and even some types of cancer (BUCHHEIT et. al., 2020).

In this sense, obesity is considered a chronic disease, which has a high incidence throughout the world, and has already reached pandemic status. In obesity, there is an accumulation of fat in adipose tissue, due to the disruption of energy homeostasis, which causes relevant damage to the individual both physically and psychologically, directly reflecting on their quality of life. To understand this process, it is observed that the energy left in the body is stored as fat, and this is metabolized when there is no carbohydrate intake. And this energy is used to support the body's functioning in a balanced way (VILARRASA et. al., 2023).

The etiology of obesity has different factors, which include interactions between genetic and endocrine factors and adverse environmental influences on health, such as poor eating habits. Obesity is considered a plurimetabolic disease as it causes complications in the body such as hypertension, dyslipidemia and diabetes. Therefore, it is a serious and predominant clinical morbidity, and as already mentioned, it has become one of the biggest health problems of the 21st century and one of the most significant causes of chronic diseases in the world.

Obesity has a series of factors that are not yet fully defined, therefore, more current research has suggested among these factors that the intestinal microbiota needs

to be observed as an influencer and even determinant in the development of this disease. Once this relationship is established, the human intestinal microbiota is considered as a metabolic organ that interferes with energy regulation, as well as insulin sensitivity, and also fat storage and, consequently, body weight (VILARRASA et. al., 2023).

This study focuses on the relationship between the microbiota and obesity because in recent research, it has been demonstrated that the greater or lesser prevalence of obesity in individuals is due to two main groups of bacteria in the intestinal flora, the bacteroidetes and the firmicutes. When considering the relevance of understanding such simple factors that can lead to obesity, consequently, whether it is also one step away from treating or preventing it, this work presents a summary of the main results and discusses how effective they are (CARVALHO et al., 2015).

The relationship between obesity and the composition of the intestinal microbiota is quite significant. It was verified in different studies with obese guinea pigs (mice), which show that obesity is largely linked to relative changes in intestinal bacteria. Such transformations affected the metabolic potential of the intestinal microbiota of these guinea pigs, for example when they are on controlled diets and there is a permeabilization of the intestinal barrier, which interferes with absorption. Thus, an intrinsic relationship is observed between obesity and the composition of the intestinal microbiota (VILARRASA et. al., 2023).

Pioneering research in this regard, carried out on humans, observed that changes in the intestinal microbiota in obese people showed that they had a greater amount of firmicutes and a smaller amount of bacteroidetes than lean people. Although this reduction in Bacteroidetes in obese people has been admitted in subsequent investigations, there is

also research that contradicts this theory of a decrease in Bacteroidetes in obese individuals. (SEGANFREDO et al., 2017).

In the national pharmaceutical market there are not many medicines approved by ANVISA to treat obesity. The release of this second one was widely celebrated by patients and health professionals, as its mode of operation is more simplified than the first. (CAPRISTO et. al., 2017)

In 2015, the marketing of injectable liraglutide was approved in the USA by the Food and Drug Administration (FDA), as a treatment option for the chronic control of obesity, and its use must be associated with a calorie-restricted diet and routine practice of physical activities, and this opened the way for other drugs in the same line, such as semaglutide. (FUJISHIMA, et. al, 2010).

The aforementioned drug was approved for use in adults, without serious illnesses and with a body mass index (BMI) equal to or greater than 30, or in patients with a BMI of 27 or greater who have at least one illness or related aggravating factor, such as high blood pressure, high cholesterol, type 2 diabetes, or dyslipidemia. In Brazil, approval by ANVISA was in 2017. (LI et. al., 2018)

Semaglutide can be considered as an analogue of incretins, specifically of the glucagon-like peptide (GLP-1), which makes up a new group of antidiabetic agents qualified for stimulating insulin secretion during the hyperglycemia process (SANZ SEGURA, P., et. al, 2023).

And in the context of this study, it is GLP-1 that regulates glucose levels, through stimulation of secretion and glucose-dependent biosynthesis, eliminates glucagon secretion, and then there is a delay in the feeling of satiety, due to the delay of gastric emptying. (GADDE et al., 2017).

Semaglutide had its safety and efficacy evaluated in three clinical experiments that covered approximately 4,800 patients with

obesity of different degrees and also overweight patients. All patients in the experiment underwent guidance sessions regarding changes in habits essential for the success of the treatment, including eating a low-calorie diet and practicing physical activity regularly. (SEIJAS-AMIGO et. al, 2023).

Therefore, the release of a drug to treat obesity is very relevant, given the reality of the increase in the number of patients with this disease and who have difficulty losing weight on their own. And the direct action of the intestinal microbiota in the weight loss process must be considered. Semaglutide is a glucagon-like peptide (GLP-1) receptor agonist that has been indicated for some time for the treatment of type 2 diabetes and has also been observed to result in considerable weight loss.

FINAL CONSIDERATIONS

This study sought to address obesity as a latent problem in modern society, and the use of medication for its treatment. The great advantage of semaglutide over most other drugs recommended for weight loss is that it has an injectable version, and the fact that it is not taken orally puts it at a certain advantage over others, as in this case the dosage is exact, the application is periodic, and there is no overdose because if the patient aims to enhance the results by applying a higher dose, this will have no effect, on the contrary, an overdose of semaglutide will cause headaches, nausea, vomiting and diarrhea, among others, but not will cause no effect on appetite.

What is evident is that the intestinal flora in both humans and animals suffers direct action from diets, being modified according to excessive calorie intake, and this triggers the propagation of bacteria from the phylum firmicutes, which allow nutrients to be extracted with more easily. This has already been proven in clinical examinations. These results lead to

a relevant context in this study, which is the possibility of manipulating the intestinal flora through drugs, which means a pharmaceutical innovation in the treatment of obesity and the complexities that surround it.

Finally, it is important to highlight that the relationship made in this study is between the intestinal microbiota and obesity, with no relationship proven in research on the effects

of semaglutide on the intestinal microbiota. It is also worth emphasizing that side effects were observed in some patients, including some more serious ones such as pancreatitis, kidney failure, gallbladder disease and suicidal thoughts. Semaglutide caused an increase in heart rate in some patients and had to be discontinued. Because of this, the cardiovascular safety of semaglutide is being studied.

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