Revista
Coleta Científica
ISSN: 2763-6496

COLETA SCIENTIFIC JOURNAL

Year V, Vol. V, n.9, Jan.-Jun., 2021

ISSN: 2763-6496

DOI: https://doi.org/10.5281/zenodo.5093482

Submission date: 02/19/2021. Acceptance date: 07/12/2021.

PHARMACOLOGY OF OBESITY AND RISKS OF DRUGS FOR WEIGHT LOSS

FARMACOLOGIA DA OBESIDADE E RISCOS DAS DROGAS PARA EMAGRECER

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Abstract
Obesity is currently considered a major public health problem, being responsible for the substantial increase in morbidity and mortality. It also presents itself as a large portion of the pharmaceutical industry, which involves the development of drugs, modified foods and also strategies that encourage dietary re-education and regular physical activity. This Literary Review sought a report on the drugs used to treat obesity and a description of their adverse side effects. Pharmacology for the treatment of obesity poses great health risks when not prescribed and monitored by qualified professionals.

Keywords: Obesity. Treatment. Medicines. Health Risks.

Resumo
A obesidade é considerada, atualmente, um grande problema de saúde pública, sendo responsável pelo aumento substancial da morbimortalidade. Ela se apresenta, ainda, como uma grande parcela da indústria farmacêutica, que envolve o desenvolvimento de fármacos, alimentos modificados e, também, estratégias que estimulam a reeducação alimentar e a prática regular de atividade física. Esta Revisão Literária buscou um relato sobre os medicamentos usados no tratamento da obesidade e a descrição de seus efeitos colaterais adversos. A farmacologia destinada ao tratamento da obesidade traz grandes riscos à saúde quando não prescrita e acompanhada por profissionais qualificados.

Palavras-chave: *Obesidade. Tratamento. Medicamentos. Risco à Saúde.*

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Introduction

Obesity is a chronic disease characterized by excessive accumulation of adipose tissue in the body. Its emergence comes from the association between genetic, metabolic, social, behavioral and cultural factors. In recent decades, it has become one of the main public health problems because, in addition to causing many health problems, it increases the risk of premature death and directly affects the quality of life. (RADAELLI; PEDROSO; MEDEIROS, 2016).

According to the World Health Organization (WHO), an individual is considered obese if the body mass index (BMI) is equal to or greater than 30 kg/m ^{2} . BMI is just an assessment tool, and in some situations it is necessary to associate other parameters. (SEGAL; FADIÑO, 2002) . The treatment of obesity has the main objective of improving health and quality of life, aiming to reduce associated diseases and subsequent mortality.

According to the World Health Organization (WHO), Brazil is one of the countries with the highest obesity rates. The main causes are attributed to poor eating habits and lack of regular physical activity, and many of these patients resort to the use of drugs to reduce appetite, seeking a "magical" weight loss, fast and effortless. (CRUZ; SANTOS, 2013).

However, Cruz and Santos (2013) emphasize that weight-loss drugs should be used as a therapeutic supplement, helping to re-educate food, change habits and practice regular physical activity, as such drugs are effective in weight control only while they are being administered, and can cause new weight gain after suspension.

The consumption of these anti - obesity drugs can be dangerous if done by people who suffer from heart diseases such as hypertension or metabolic disorders and must be indicated by a specialist doctor, after physical evaluation, ruling out the presence of insulin resistance, thyroid changes or heart problems, should be accompanied by a hypocaloric diet and regular physical exercise. (SANTOS et al. 2019)

Therefore, this literature review study aims to highlight the importance of pharmacology in obesity and the risks that the indiscriminate use of drugs to lose weight represent, at the expense of the health and quality of life of the user.

Methods

This is a Literature Review work based on scientific articles published in the last ten years in free databases on the internet, such as Scielo , LILACS, BVS, Pubmed , Ministry of Health publications, Google academic and virtual libraries. The descriptors used as inclusion criteria in the sample were: obesity, prevention, medication, health risks.

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Results and discussion

Obesity

Obesity is a medical condition caused by the accumulation of body fat. One of the main causes of obesity is the exaggerated intake of calories, when there is no balance between the energy that is ingested in the form of food and the energy that is spent in everyday activities. (TAVARES; NUNES; SANTOS, 2010).

The increase in obesity is associated with a sedentary lifestyle and a diet rich in fats and additives, which favor the onset of chronic diseases such as lipid and cardiovascular disorders, changes in glucose metabolism, sleep apnea , orthopedic problems, polycystic ovary syndrome and metabolic syndromes. . Another worrying factor, especially among young females, concerns the socioeconomic and cultural pressures associated with the aesthetic standards of the time, in view of the growing emphasis on thinness as aspects associated with beauty standards. (QUEIROZ, 2013).

According to Bolsoni- Lopes et al. (2021), the growth of obesity in the last three decades has reached more than 650 million people in the world, it is considered a chronic and inflammatory disease, caused by the increase in adipose mass. In a reflective analysis, these authors suggest that the severity of many current diseases, including Covid-19, is directly associated with an increase in BMI, also indicating that obesity may be a risk factor for morbidity and mortality from SARs-infection. COV2, regardless of association or not with other comorbidities .

In the understanding of several health professionals, the physiological mechanisms that connect obesity and Covid-19 are crucial for the adequate care of the disease. It is worth remembering that adipose tissue is the regulatory center of body metabolism, being an endocrine organ that produces hormones, adipokines and cytokines . In the assessments of health professionals, it is emphasized that obesity would be contributing to the increase in infections by SARs-COV2, namely: amplification of the state of inflammation, damage to the respiratory and cardiovascular systems and glucose metabolism, favoring the formation of thrombus and dysregulation of the immune system. (BOLSONI-LOPES et al. 2021

Obesity Pharmacotherapy

In the treatment of obesity, non-pharmacological and pharmacological therapeutic forms are fundamental. Non-pharmacological measures are evidenced in behavioral therapies, changes in eating habits, physical activity and guidance from a professional nutritionist, in order to reduce caloric consumption. Pharmacological measures should be used in the treatment of obesity, when there are therapeutic failures in the non-pharmacological alternative, and when the patient has comorbidities associated with obesity or in cases of obesity type II and III. (COSTA; DUARTE, 2017).

The therapeutic pharmacology of obesity has undergone profound changes over the last few decades, especially due to the development of new drugs and non-

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pharmacological treatment proposals. Currently, pharmacological therapy is indicated in cases where patients have a body mass index (BMI) greater than 30. BMI is obtained by dividing the patient's (weight/height ^{2}). The pharmacological indication should occur when the patient has diseases associated with excess weight. (NEGREIROS et al. 2011).

pharmacotherapy consensus, it is recommended that slimming drugs are always used in conjunction with a lifestyle change program, such as helping to change eating habits and regular practice of physical activities. It is emphasized that drugs should only be used under medical supervision and after a careful assessment of the risk-benefit balance for each specific patient. (COUTINHO; CABRAL 2000) .

drugs to lose weight

Anorectic medications, also known as appetite suppressants, are drugs that cause a reduction or loss of appetite. They are not recommended as a single treatment for weight loss, as they act on the Central Nervous System and cause effects on mental and behavioral function. (CAMELO; DINELLY; OLIVEIRA, 2016).

It is essential that the user has a prescription and medical and pharmaceutical guidance in order to be aware of the risks and benefits of anorectic drugs and possible drug interactions, in addition to the problems related to the incorrect use of drugs. Through professional guidance, medication should be combined with non-pharmacological methods, such as physical exercise and patients' dietary reeducation. The interaction between patient, pharmacist and doctor is an important factor in the pursuit of patient health and well-being. (TAVARES, ANGELO; SOUZA, 2017).

In Brazil, the five drugs registered for the intervention of obesity, that is, the drugs most used in the weight loss process, are divided into two groups: those that minimize hunger (amfepramone , fenproporex and mazindol) or alter satiety (sibutramine) and those that decrease digestion and nutrient absorption (orlistat). (SOUZA et al, 2017).

Originally, *amfepramone* (diethylpropion) was developed for the treatment of narcolepsy and, in contradiction, for children with hyperkinesia . Its side effect is appetite suppressant, and then it is used as an anorectic drug. (NACCARATO, LAKE, 2014).

Amphepramone is a derivative of β- phenethylamine acting on the central nervous system through several mechanisms of action that act on different receptors such as epinephrine , serotonin, dopamine and norepinephrine . This drug acts by increasing the release of monoamines , inhibiting the enzyme monoamine oxidase and favoring the synthesis of neurotransmitters. Additionally, it inhibits the reuptake of serotonin, at a lower intensity, due to the removal of the neurotransmitter from its presynaptic transporter. (PEREIRA; SOUZA, 2017).

However, the use of amfepramone can promote adverse reactions such as cardiac arrhythmia, nervousness, insomnia, hallucinations, psychotic conditions, tachycardia, abdominal pain, vomiting, nausea, decreased libido, arterial

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hypertension, diarrhea, chills, pallor, excitement, dry mouth, decrease in sexual potency, and should be used with great care. (PEREIRA et al, 2012).

Femproporex is classified as an indirect-acting dopaminergic agent and acts by stimulating or inhibiting the *neuronal* reuptake of norepinephrine and dopamine in the synaptic cleft. The anorectic action occurs in the hypothalamic control center, causing an increase in catecholamine release from neural terminals and/or inhibition of reuptake . As a result, its psychostimulant effect suppresses appetite by voluntarily reducing food intake and reducing the activity of the gastrointestinal tract. (MARCON et al, 2012). The substance also has central effects that cause locomotor stimulation, state of excitability, euphoria, stereotyped behavior and anorexia. In moderate doses, it induces a feeling of well-being , increased concentration, interlocution and psychomotor improvement. (KONFLANZ; SILVA; DALLANGNOL, 2014).

The following side effects caused by the use of fenproporex have been reported : anxiety, insomnia, hallucinations, tremors, mental confusion and agitation, in addition to symptoms of depression, nausea, headache , dysphoria and fatigue (ESPOSTI, 2017).

Mazindol is a tricyclic amphetamine derivative used in the treatment of obesity and its consumption has already reached high levels in several countries. (KOEDA et al. 2017; LUCAS; TEIXEIRA; OLIVEIRA, 2021). Its anorectic action occurs by catecholaminergic action, being effective for weight loss and is widely used in obesity in association with hypocaloric diets.

This drug blocks the reuptake of serotonin and norepinephrine , in addition to inhibiting dopamine. This action causes the blockage of the production of gastric secretion, favoring the reduction of appetite. It is assumed that the hypothalamic action of mazindol causes the cancellation of the desire to ingest food, decreasing glucose absorption and intensifying locomotor activity (GONÇALVES et al, 2014).

The side effect of mazindol is similar to that of other anorectics, and therapeutic doses can cause constipation, dry mouth, tachycardia, irritability, among others. (BEHAR, 2002).

Sibutramine, initially developed as an antidepressant, was the first drug used in anti- obesity treatment , as during some tests, it was found that the substance was capable of reducing appetite. (COSTA; DUARTE 2017).

Some studies consider that sibutramine can improve the lipid profile of patients. This effect, associated with weight loss, can be a great ally in the fight against obesity-associated comorbidities (CAMPOS et al, 2018).

The use of sibutramine in hypertensive patients is recommended with great caution, with extensive monitoring of the patient's blood pressure until the end of treatment . Its use is contraindicated in patients who have coronary or peripheral artery disease, stroke and uncontrolled arterial hypertension. It is also not indicated for individuals who have diseases related to the central nervous system (LIMA et al., 2018; LUCAS; TEIXEIRA; OLIVEIRA, 2021).

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The most frequent adverse effects of sibutramine are headache, dry mouth, constipation, insomnia and high blood pressure. The most common side effects occur in 10 to 20% of cases. (FORTES et al, 2006).

The use of orlistat is related to weight loss through significant reductions in systolic and diastolic blood pressure. The use of the drug must be with caloric-fat restrictions, which demonstrates weight loss in obese non-diabetic individuals, insulinemic reductions and glycemia reductions. With no central effect, it becomes a considerable choice in patients with psychiatric disorders and who use antidepressant drugs (SOUZA et al, 2017).

Orlistat has specific action on gastric and pancreatic lipases, functioning as a potent inhibitor . Lipases are catalysts for the hydrolytic removal of fatty acids from triglycerides, resulting in free fatty acids and monoglycerides . Orlistat covalently and irreversibly binds to the active sites of lipases, allowing one third of the triglycerides to be excreted without undergoing digestion, not undergoing absorption in the small intestine with consequent elimination in the feces. (OLIVEIRA et al, 2009).

The main side effects of orlistat are: diarrhea , decreased absorption of fat-soluble vitamins, abdominal pain, flatulence and incontinence. (RIBEIRO, 2014).

health risks

The increase in overweight and obese individuals has been growing along with the search for an ideal body, which ends up causing the exaggerated and inappropriate use of appetite suppressants. However, appetite suppressant drugs should not be used only for aesthetic purposes, due to their side effects (ANDRADE et al, 2019). The uncontrolled use of these anti - obesity drugs can cause increased bacterial resistance through misuse and even brain hemorrhage due to the combination of an anticoagulant and an analgesic. (DUTRA; SOUZA; PEIXOTO, 2015).

Treatment with appetite suppressants is currently in the profile of drugs administered irrationally and exaggeratedly. Often, the drug is prescribed by certain doctors without any indication or information about concomitant treatments, such as dietary reeducation and physical activity. (CASSIN, 2018).

Almeida et al (2012) highlights that drugs are substances that can bring side effects and serious damage to health in the form of severe and/or moderate adverse reactions. Adverse reactions in children and adolescents are especially important as they can interfere with their physical and cognitive development.

In the Brazilian population, self-medication is a common practice, and individuals are usually exposed to the indiscriminate use of medication through indications from family, friends or the media. One should not underestimate the influence of fashion and culture, which can encourage the use of medicines for aesthetic reasons, such as drugs used to lose weight or gain muscle mass. (ALMEIDA et al, 2012).

According to Chaud and Marchioni (2004), anti- obesity drugs help with weight loss, but they can produce dangerous side effects. Even food supplements

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and vitamins must be prescribed by a doctor, who will be able to correctly guide the treatment. Such medications, when taken without professional guidance, can be highly harmful, causing accelerated cardiac risk, increased blood pressure, cardiovascular risk, fatigue and even glaucoma.

In Brazil, the indiscriminate use of drugs to lose weight has been growing more and more, as has the sales of these drugs without a prescription, such as: appetite suppressants, laxatives, diuretics, hormones and manipulated products. Both users and health professionals should be aware that many of these drugs, after a few months, lose their effectiveness, causing a rebound effect where people gain weight again, which can also lead to other harmful health effects. (BRAZIL, 2002).

Final considerations

Obesity has been getting worse in Brazil and in the world, bringing with it many risks to the health of the individual. Pharmacological treatment alone does not bring about a cure for obesity, being necessary and essential the association with dietary reeducation and physical activity, in addition to changes in habits and lifestyle.

However, the treatment for obesity must happen under the guidance of a qualified professional, who can evaluate, prescribe and monitor the use of drugs to lose weight.

Many of the drugs to lose weight have an extremely delicate action on the body, acting on the central nervous system, on the brain nucleus responsible for hunger, the hypothalamus. Such a mechanism can cause dangerous side effects, which include palpitations, insomnia, increased blood pressure, and even drug addiction.

On the other hand, indiscriminate use or without professional guidance can encourage practices that put the patient's health and quality of life at risk.

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