

## **USE OF iSGLT2 IN THE TREATMENT OF PATIENTS WITH HEART FAILURE AND DIABETES MELLITUS**

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**Abstract: Purpose:** to evaluate the favorable and unfavorable results in the use of sodium glucose-SGLT2 cotransporter inhibitors such as empagliflozin and dapagliflozin in the treatment of type 2 diabetes mellitus (DM2) and heart failure (HF) patients **Methods:** An integrative review was carried out, using as criteria the search in the National Library of Medicine (PubMed) and Scientific Electronic Library Online (SciELO) databases using the descriptors (i) iSGLT2 (ii) Heart failure, (iii) Diabetes mellitus, with the Boolean operator “AND”. Studies published from 2018 to 2023 were included. **Results:** There is a need for better therapies to reduce damage to target organs and symptoms. A group of drugs that have shown promise are the type II sodium glucose cotransporter inhibitors, studies show that dapagliflozin mainly reduced cardiovascular risks and death from cardiovascular causes in patients with heart failure, reducing renal outcomes, with the latest anti-diabetic drugs approved by the Food and Drug Administration (FDA) with high efficacy for the control of both pathologies and which are safe to use, reducing negative outcomes, allowing these patients to have a better quality of life.

**Keywords:** SGLT2, Heart failure, Diabetes mellitus.

## INTRODUCTION

Type 2 diabetes mellitus (DM2) is a chronic metabolic disorder characterized by persistent hyperglycemia initially associated with hyperinsulinism that later reverts to little or no insulin secretion, due to the fatigue of the pancreatic beta cells, being responsible for a large part of the world morbidity and mortality (GARNICA-CUÉLLAR et al., 2022).

As far as heart failure is concerned, we know that it is a chronic disease characterized as a syndrome that leads to the inability of the

heart to act effectively as a pump, either due to a contraction deficit or muscle relaxation, leading to injuries like diabetes. of target organs and a worsening in the quality of life of these patients (Solomonet al.,2022).

Being two pathologies that usually run together and affect thousands and thousands of people each year, there is a need for drugs that improve the symptoms of patients affected by these pathologies, where today we have iSGLT2 on the market. (REQUENA-IBÁÑEZ et al.al.,2022).

Acting on the type II sodium glucose cotransporter, where they inhibit the absorption of glucose in the proximal convoluted tubule whose end result is glycosuria and the reduction of blood glucose levels, however this effect does not explain its benefit in the treatment of patients with heart failure. ( BOCCHI etal.,2021).

Its benefit does not seem to be directly related to the reduction of blood pressure levels and dyslipidemias, since when EMPAREG studies were carried out, no correlation was observed with the metabolic profile or even hemodynamics of these patients. (BOCCHI e tal.,2021).

Among the most accepted mechanisms to explain the mechanism of action of SGLT2 in HF is the reduction of left ventricular parietal pressure by decreasing preload and afterload, which makes it a promising drug for this group of patients and of very high interest. from study to scientific Society. (BOCCHI et al.,2021).

## **REVISION**

### **INCIDENCE AND PREVALENCE**

Both pathologies currently reach epidemic proportions and have become a public health problem not only in Brazil but worldwide, approximately 415 million people between 20 and 79 years old have diabetes and it is expected that this number will reach 615

million in 2040 (FONTES-CARVALHO et al., 2022).

Brazil is now the fifth country in the world with the highest incidence of diabetes, with 16.8 million patients between 20 and 79 years of age, second only to China, India, the United States and Pakistan (GREGORY et al., 2022).

When the situation of Brazilians with heart failure is shown, the picture is not very different, reaching an incidence of 240,000 new cases per year and a prevalence of 2 million patients (LORENZO et al., 2022).

### **PATHOPHYSIOLOGY**

Type 2 diabetes mellitus can develop by two mechanisms, either persistent hyperglycemia or a deficiency in insulin production, being classified into two groups according to the cause, where in type II a strong peripheral resistance to insulin, which generates an increase in Insulin demand culminating in a depletion by these cells in patients with advanced disease, however, there are other causes of hypoinsulinism such as low GLUT2 expression in cell membranes and deficiencies of incretins, both of which are little known (SHARMA et al., 2022).

In heart failure we have the pathophysiology of heart failure as a pump to meet organic and tissue needs, where the elevation of pulmonary venous pressure-PVP or systemic that results in congestion of various organs, which usually occurs due to cardiac systolic or diastolic dysfunctions, more as in most cases it occurs in both parts of the cycle, leading to cardiomyocyte remodeling. (FERNANDO et al., 2022).

### **RISK FACTORS**

Both share the same risk factors, whether modifiable or non-modifiable, among them are advanced age, duration of DM and HF, poor glycemic and blood pressure control, poor medication adherence, failure to change

lifestyle-SEM which includes a healthy diet, patients with a high body mass index-BMI, presence of microalbuminuria, and the presence of other concomitant comorbidities (ANGELES et al., 2022).

### SIGNS AND SYMPTOMS

Symptoms are diverse ranging from local or systemic symptoms, having symptoms such as tiredness, weakness, blurred vision, and symptoms that are characteristic of diabetes such as polyphagia due to non-use of glucose by the cell, polydipsia due to the large amount of glucose in the blood increases osmolarity, which leads to the activation of receptors sensitive to osmolar alteration, generating thirst, weight loss due to deprivation of glucose consumption by the cell and also due to some medications used to control diabetes mellitus (fan e tal., 2022).

Insufficiency shares some symptoms with diabetes, such as tiredness and weakness, but it remains with the particular symptoms such as dyspnea, edema of the lower limbs, hepatomegaly, cough with frothy and sometimes pink secretion, nocturia and, in more advanced stages, mental confusion. (SALOMON et al., 2022).

### CLASSIFICATION

Diabetes mellitus is currently classified into 4 main subtypes listed below

TYPE 1 DIABETES
TYPE 2 DIABETES
GESTATIONAL DIABETES
OTHER TYPES OF DIABETES

TABLE 1. Elaborated by the authors.

NEW YORK HEART ASSOCIATION CLASSIFICATION	
I	Absence of symptoms during activities
II	Symptoms in everyday activities
III	Symptoms on minor exertion
IV	symptoms at rest

TABLE 2. Elaborated by the authors.

EJECTION FRACTION	PERCENTAGE
ICFEr	<40%
ICFEi	40-49%
ICFEp	>50%

TABLE 3. Elaborated by the authors.

### DIAGNOSIS

The diagnosis of heart failure is clinical, made through the clinical history reported by the patient, such as the inability to make efforts, dyspnea and edema of the lower limbs, as well as a physical examination that demonstrates the accumulation of blood in the lungs and in the body, the confirmatory examination being echocardiogram and laboratory tests, such as the production of B-type natriuretic peptide, also called BNP, which is fundamental in the laboratory diagnosis of heart failure (GONZÁLEZ-JUANATEY et al., 2022).

The diagnosis of Type II Diabetes Mellitus is based on a laboratory analysis with simple and routine tests for most Brazilians, such as fasting blood glucose, oral glucose tolerance test or even glycated hemoglobin, requiring two different tests for confirmation. diagnosis, with an exception to the rule where if the patient has undeniable symptoms of diabetes associated with an altered test, the diagnosis is confirmed. (FRALICK et al., 2022).

## NEW THERAPEUTIC

In view of the large number of patients affected by these pathologies, there is a need for better therapies, to reduce damage and symptoms associated with an increase in survival, a group of drugs that have shown promise are the type II sodium-glucose cotransport inhibitors, which within this class are dapagliflozin and empagliflozin (butt et al., 2022).

Where studies show that mainly dapagliflozin reduced cardiovascular risks and death from cardiovascular causes in patients with heart failure, reducing renal outcomes, demonstrated a reduction in the progression of the glomerular filtration rate either due to hypertensive or diabetic disease, whereas empagliflozin obtained an isolated reduction in progression of the decline in GFR. (VILLAGRAN et al., 2022).

Both are considered safe drugs for use by the FDA, and are also safe for use in the elderly, provided that correct monitoring is carried out in order to avoid dehydration and hypotension, always taking into account the degree of fragility of each patient in the prescription, and it is better to start it in low doses. (VILLAGRAN et al., 2022).

## FUTURE PERSPECTIVES

Although the quality of care for diabetic patients and patients with heart diseases has improved, there is still much to improve, modifying health services and medicines, with sodium glucose type II cotransport inhibitors - SGLT2 being the latest antidiabetic drugs that received approval by the Food and Drug Administration (FDA), with high efficacy for the control of both pathologies and which are safe to use, reducing negative outcomes, allowing these patients to have a better quality of life (NOLAN et al., 2022).

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