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FLOZINS - MODERN TREATMENT FOR PATIENTS WITH TYPE 2 DIABETES

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Abstract

Introduction:

Type 2 diabetes is a metabolic disease characterized by elevated blood glucose levels. Uncontrolled disease leads to many complications that significantly affect quality of life and life expectancy. Flozins – sodium-glucose cotransporter 2 (SGLT2) inhibitors are a new group of drugs used in the treatment of DM 2, which, in addition to their hypoglycemic effect in the form of increased glucose excretion in urine, also have a beneficial effect on the cardiovascular system.

Objective:

The aim of the study was to present the benefits of using SGLT2 inhibitors in patients with type 2 diabetes.

Materials and methods:

We reviewed the literature in PubMed using the keywords: “Diabetes type 2”, “Flozins”, “SGLT2 inhibitors”, “Cardiovascular disease”, and “Renal disease”.

Results:

It has been proven that SGLT2 inhibitors, in addition to their hypoglycemic effect, also have a beneficial effect on other systems. The studies discussed show that SGLT2 drugs reduce cardiovascular risk and have a protective effect on the kidneys.

Summary:

The efficacy of SGLT2 inhibitors therapy has been confirmed in clinical trials. Future studies should aim to determine at what stage treatment should be initiated in order to maximize the benefits for the patient.

Keywords: type 2 diabetes, flozins, SGLT2 inhibitors, cardiovascular disease, renal disease.

1. Introduction.

Flozins, or SGLT2 inhibitors, are a new class of antidiabetic drugs that are revolutionizing the treatment of type 2 diabetes and the heart and kidney diseases that often accompany it. The history of flozins dates back to 1835, when French chemist C. Petersen isolated phlorizin from the root bark of apple trees. Phlorizin was the first known flozin, but its poor bioavailability prevented its use in the treatment of diabetes. In the 1990s, Japanese researchers developed the first synthetic SGLT2 inhibitors that were effective when taken orally. The first approved drugs in this class were canagliflozin (2013), dapagliflozin (2014), and empagliflozin (2014), developed by pharmaceutical companies such as Johnson & Johnson, AstraZeneca, Boehringer Ingelheim, and Eli Lilly. Flozins are a modern and effective form of therapy for several reasons. First, their unique mechanism of action involves inhibiting glucose reabsorption in the kidneys, which leads to lower blood sugar levels without the risk of hypoglycemia. In addition, flozins have cardiovascular benefits that have been confirmed in numerous clinical trials.

2. Mechanism of action of SGLT2 inhibitors.

The mechanism of action of flozins is based on the inhibition of sodium-glucose cotransporter 2 (SGLT2) in the proximal tubules of the kidneys. This transporter is responsible for the reabsorption of approximately 90% of glucose from primary urine. By blocking SGLT2, flozins increase glucose excretion in urine, leading to a condition known as glucosuria. Glucose excretion by the kidneys increases by up to 50-80 g/day[1]. This effect is independent of insulin, which is why these drugs are also effective in people with reduced sensitivity to this hormone[2].

Glucosuria induced by SGLT2 inhibitors leads to calorie loss. This effect promotes weight loss, which averages 2.5–3 kg[3]. In addition, the renal threshold for glucose is reduced, resulting in a decrease in blood glucose levels[4]. Flozins reduce insulin secretion and increase sensitivity to this hormone. This phenomenon is beneficial for the function of pancreatic β cells[5]. In turn, pancreatic α cells are inhibited from secreting glucagon. Thus, hepatic gluconeogenesis increases, but the hypoglycemic effect is not eliminated[6].

SGLT2 inhibitors also affect the body's energy profile. They induce a state of pseudo-starvation and increase the production of ketone bodies (such as β-hydroxybutyric acid) by up to 20-30%. Ketones become an alternative source of energy for the heart, which improves its efficiency[7,8]. In addition, flozins reduce triglyceride concentrations and increase HDL levels, thus having a beneficial effect on the lipid profile[9].

Through hemodynamic mechanisms such as osmotic diuresis and natriuresis, sodium is lost and plasma volume is reduced[10]. This, in turn, reduces the preload and afterload on the heart. Blood pressure decreases[11]. The cardioprotective effects of SGLT2 inhibitors result from improved endothelial function, inhibition of cardiac remodeling, and changes in energy substrates. This increases the metabolic efficiency of the heart[12].

Flozins also have a nephroprotective effect. They slow down the decline in glomerular filtration and inhibit hyperfiltration by acting on TGF-β (transforming growth factor beta)[13]. In addition, they have anti-inflammatory and anti-fibrotic effects. They reduce pro-inflammatory cytokines (such as IL-6, TNF-α) and inhibit macrophage activation. They reduce fibrin expression in the vascular endothelium[14].

All these mechanisms make SGLT2 inhibitors breakthrough drugs in the treatment of diabetes and cardiovascular diseases. They offer benefits not only in terms of glycemic control, but also in protecting the heart and kidneys.

3. Benefits of SGLT2 use described in studies.

The EMPA-REG OUTCOME study demonstrated the efficacy of empagliflozin in reducing the risk of cardiovascular death and other complications in patients with type 2 diabetes and high cardiovascular risk. It was conducted on over 7,000 patients with type 2 diabetes and a high risk of cardiovascular disease from 42 countries. It was a randomized, double-blind study that evaluated the effect of empagliflozin on cardiovascular events compared to placebo. The results showed that empagliflozin 10 mg or 25 mg once daily, in combination with standard treatment, resulted in a significant reduction in cardiovascular deaths by 38% compared to placebo. In addition, the study showed a 35% reduction in hospitalizations for heart failure. Empagliflozin also contributed to a 32% reduction in overall mortality. These results are of great importance to medicine, as this is the first time that an oral antidiabetic drug has been shown to reduce both cardiovascular and overall mortality[15,16].

The CANVAS (Canagliflozin Cardiovascular Assessment Study) evaluated the efficacy and safety of canagliflozin in reducing the risk of cardiovascular events in patients with type 2 diabetes. Canagliflozin has been shown to reduce the risk of major cardiovascular events, such as cardiovascular death, myocardial infarction, and non-fatal stroke, by 14% compared to the placebo group. In addition, the CANVAS study revealed beneficial effects of treatment on kidney function. Analysis of renal endpoints showed that canagliflozin reduces the risk of events such as the need for renal replacement therapy and renal deaths. Detailed analysis also showed a significant reduction in the risk of doubling creatinine levels. These results confirm the nephroprotective effect of the treatment, which is important for patients with diabetes and kidney disease[17].

The DECLARE-TIMI 58 study is another important analysis that evaluated the effect of dapagliflozin on the risk of cardiovascular events in patients with type 2 diabetes. The

results of the study showed that dapagliflozin reduces the risk of cardiovascular death or hospitalization for heart failure by 17%. A detailed analysis shows that the incidence of these events was lower in the dapagliflozin-treated group (4.9%) compared to the placebo group (5.8%). In addition, the DECLARE-TIMI 58 study revealed a beneficial effect of dapagliflozin on kidney function. Treatment reduces the risk of worsening of the estimated glomerular filtration rate (eGFR) by ≥40%. This suggests that dapagliflozin not only protects the heart but also has the potential to protect the kidneys[18,19].

4. Side effects of SGLT2 inhibitor treatment.

Despite their effectiveness in lowering blood sugar levels and their cardiological benefits, flozins can cause certain side effects. The most common side effects include bacterial urinary tract infections. Elevated glucose levels in the urine provide a breeding ground for bacteria, which promotes their growth in the urinary tract. These affect women in particular and are associated with increased glucose excretion in the urine. In rare cases, these infections can lead to more serious complications, such as pyelonephritis, which requires intensive antibiotic treatment and may be an indication for discontinuation of therapy[20]. Fungal infections of the genital organs may occur with similar frequency. Increased glucose excretion in urine creates an ideal environment for fungal growth[21]. Hypoglycemia may occur during treatment. The risk of this occurring is higher when flozins are used in combination with other antidiabetic drugs, such as insulin or sulfonylureas[22]. Increased diuresis may cause more frequent urination and dry mouth. Hypotension, on the other hand, may lead to dizziness and weakness[23]. A very rare but serious side effect is Fournier's gangrene. This is an extremely serious bacterial infection of the soft tissues of the perineum and genitals. This disease can progress rapidly and require hospitalization, numerous surgical procedures, and can even lead to death[24].

5. Summary.

The studies and analyses discussed above clearly show a number of benefits of using SGLT2. Drugs in this group offer new hope for patients with type 2 diabetes. They offer

benefits in terms of both glycemic control and heart and kidney protection. Future studies should aim to determine at what stage treatment should be started in order to maximize the positive outcomes of therapy for the patient. Unfortunately, drugs in this group may cause some side effects, but these can be minimized through appropriate prevention and early treatment.

Disclosure

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