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Effects of SGLT2 (Sodium-Dependent Type 2 Glucose Transporters) on Different Systems

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ABSTRACT

SGLT2 inhibitors are a class of drugs commonly used in the treatment of type 2 diabetes. Although these drugs are effective in controlling blood sugar, they also have significant systemic side effects that must be considered. The most common side effects of SGLT2 inhibitors include urinary tract infections, euglycemic ketoacidosis, orthostatic hypotension, dehydration, and cardiovascular adverse events. In addition, an increased incidence of bone fractures and decreased bone mineral density has been observed in patients taking these drugs.

It is important that physicians consider these side effects when prescribing SGLT2 inhibitors and monitor patients regularly for any complications. Individual benefit-risk assessment is critical before deciding to prescribe these drugs. In summary, although SGLT2 inhibitors are an effective treatment option for type 2 diabetes, their use should be carefully evaluated and monitored to minimize systemic side effects.

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INTRODUCTION

SGLT2 (sodium-dependent glucose transporters type 2) are membrane proteins found in cells of the proximal renal epithelium. These proteins play an important role in the regulation of glucose balance in the human body.1

SGLT2 is responsible for the reabsorption of filtered glucose in the kidneys, which means that it helps to recover glucose that is eliminated through urine and returns it to the bloodstream. This is done by uptake of glucose into the lumen of the renal tubule through the luminal membrane of the epithelial cell and its transport across the epithelial cell into the blood through the basolateral membrane.1

SGLT2 inhibitors are a class of anti-diabetic drugs that work by blocking the action of SGLT2. By inhibiting glucose reabsorption in the kidneys, these drugs increase glucose elimination in the urine, which helps reduce blood glucose levels in patients with type 2 diabetes.1

However, there are also potential side effects of SGLT2 inhibitors, including urinary tract infections, diabetic ketoacidosis, hypotension, dehydration, and increased risk of bone fractures. Therefore, it is important that patients discuss these risks with their physician before starting treatment with SGLT2 inhibitors.1

NEUROLOGICAL EFFECTS

Neurological side effects associated with SGLT2 inhibitors are rare, but may occur in very rare cases. Some of these side effects may include:2

Encephalopathy: Encephalopathy is a general term referring to a disorder in brain function. Rare cases of encephalopathy have been reported in association with the use of SGLT2 inhibitors. Symptoms may include confusion, drowsiness, disorientation, agitation, and memory problems.2

Seizures: Rare cases of seizures have been reported in patients treated with SGLT2 inhibitors. Patients who have a history of seizures or who take other medications that may increase the risk of seizures, such as antipsychotics, may be at increased risk.2

Hypoglycemia: Hypoglycemia is a common side effect of many diabetes medications, including SGLT2 inhibitors.

Hypoglycemia can cause neurological symptoms, such as tremors, sweating, confusion and visual disturbances.2

Peripheral neuropathy: Peripheral neuropathy is a disorder that affects nerves outside the brain and spinal cord. Rare cases of peripheral neuropathy have been reported in association with the use of SGLT2 inhibitors. Symptoms may include pain, numbness, tingling and weakness in the extremities.3

It is important to note that these neurological side effects are rare and generally occur in patients with other risk factors. 4

CARDIAC EFFECTS

SGLT2 inhibitors have been associated with a number of both positive and negative cardiac side effects. Some of the more common cardiac side effects are described below:5

Reduced cardiovascular mortality: SGLT2 inhibitors, such as empagliflozin and canagliflozin, have been shown to significantly reduce cardiovascular mortality in patients with type 2 diabetes and established cardiovascular disease.5

Risk of heart failure: In some studies, an increased risk of heart failure has been observed in patients treated with SGLT2 inhibitors. However, SGLT2 inhibitors have also been shown to reduce the risk of hospitalization for heart failure in patients with cardiovascular disease and type 2 diabetes.5

Increased risk of cardiovascular adverse events: In some studies, an increased risk of cardiovascular adverse events, such as myocardial infarction and stroke, has been observed in patients treated with SGLT2 inhibitors. However, this risk appears to be lower in patients with established cardiovascular disease than in those without cardiovascular disease.6,7

Diabetic ketoacidosis: Diabetic ketoacidosis is a serious complication of diabetes that can lead to hospitalization and even death. Although a rare side effect, an increased risk of diabetic ketoacidosis has been reported in patients treated with SGLT2 inhibitors.8,9

ENDOCRINOLOGICAL EFFECTS

Euglycemic ketoacidosis is a rare but serious complication that has been associated with the use of sodium-glucose cotransporter type 2 (SGLT2) inhibitors. This condition is characterized by an accumulation of ketone bodies in the blood at elevated levels without significant elevation of blood glucose levels.9,10

Unlike classic diabetic ketoacidosis, which occurs in the setting of significant hyperglycemia, euglycemic ketoacidosis occurs in patients with diabetes who have normal or only slightly elevated blood glucose levels. This can make the condition difficult to diagnose and treat, as physicians may not consider the possibility of ketoacidosis in patients with normal blood glucose levels.10

Although euglycemic ketoacidosis is rare, it can be a serious complication that requires immediate medical attention. Symptoms may include nausea, vomiting, abdominal pain, shortness of breath, confusion and lethargy. If left untreated, euglycemic ketoacidosis can lead to diabetic coma and can be life-threatening.10

It is believed that SGLT2 inhibitors may contribute to euglycemic ketoacidosis by reducing insulin levels and increasing levels of counterregulatory hormones, such as glucagon and catecholamines. These hormones may stimulate the production of ketone bodies in the liver and reduce glucose utilization by peripheral tissues, which may contribute to an accumulation of ketone bodies in the blood.10

It is important to note that euglycemic ketoacidosis is a rare side effect of SGLT2 inhibitors, but it can be a serious complication. Patients taking these medications should watch for symptoms of ketoacidosis, even if they have normal blood glucose levels, and seek medical attention immediately if they experience any of these symptoms.11

Gastrointestinal Effects

Of course, the most common gastrointestinal side effects associated with SGLT2 inhibitors include nausea, vomiting, diarrhea and abdominal pain. These symptoms may be caused by increased glucose content in the intestine, which in turn leads to increased fluid flow to the intestine and increases intestinal motility. Fortunately, these side effects are usually mild and disappear in a short time as the body becomes accustomed to the drug.11

Genitourinary Effects

Some people may also experience urinary tract infections (UTIs) due to the elimination of glucose in the urine, which creates a favorable environment for bacterial growth. The FDA has issued a warning about the risk of serious and recurrent genital and urinary tract infections with the use of SGLT2 inhibitors, especially in women. People taking these drugs are advised to maintain good genital hygiene and to inform their physician if they experience symptoms of UTIs, such as pain or burning with urination, frequent urination, fever, or lower abdominal pain.11

BONE EFFECTS

SGLT2 inhibitors have been shown to decrease calcium reabsorption in the kidneys and increase calcium excretion in the urine. This may lead to decreased bone mineral density and increase the risk of bone fractures. In addition, SGLT2 inhibitors have been shown to increase parathyroid hormone levels, which may also contribute to decreased bone mineral density.12

However, studies on the bone side effects of SGLT2 inhibitors have yielded conflicting results, and it is unclear whether these drugs increase the risk of fractures in all patients or only in those with pre-existing risk factors.12

In a recent study, the use of SGLT2 inhibitors was found to be associated with an increased risk of foot and long bone fractures in patients with type 2 diabetes. However, another study found that SGLT2 inhibitors did not increase the risk of bone fractures in patients with type 2 diabetes.13,14

It is important to note that the bone side effects of SGLT2 inhibitors are not yet fully understood and further studies are needed to determine the actual risk of bone fractures associated with these drugs. 15

CONCLUSIONS

In conclusion, SGLT2 inhibitors are an effective class of drugs in the treatment of type 2 diabetes, but they also have systemic side effects that must be considered. Common side effects include urinary tract infections, euglycemic ketoacidosis, orthostatic hypotension, dehydration, and cardiovascular adverse events.

In addition, an increased incidence of bone fractures and decreased bone mineral density has been observed in patients taking these drugs. It is important to take these side effects into account when prescribing SGLT2 inhibitors and to monitor patients regularly for any complications. In general, the benefits and risks should be evaluated individually for each patient before deciding to prescribe these drugs.

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