What Are the Benefits in the Association of SGLT2 Inhibitors and Other Drugs

COMMENTARY

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Abstract

The SGLT2 inhibitors are a class of drugs that blocks the sodium-glucose co-transport, which is responsible for 90% of the nephron glucose. Objective: To show the benefits of the SGLT2 inhibitors in monotherapy and in association with other drugs. Results: The association of SGLT2 inhibitors and other drugs has shown several additional benefits after their interaction, including weight loss, reduction of body fat, reduction of triglycerides level, decrease of glycated hemoglobin, decrease in postprandial glucose level, reduction of arterial pressure, decrease of hypoglycemia risk and improvement of glucose metabolism. Therefore, this is a promising interaction for type 2 diabetes.

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Keywords

SGLT2; Inhibitors; Drugs.

The SGLT2 inhibitors block the sodium-glucose co-transport type 2, which is responsible for the reabsorption of 90% of the glucose in kidneys, promoting glycosuria and, consequently, the control of type 2 diabetes [1].

The action mechanism is independent of insulin and pancreatic function, therefore, it represents a real promise as anti-diabetic oral drugs, once they provide a better management of glycemic level, without the augment of the risk of hypoglycemia, and promotes weight loss [2].

Chen et al., 2016 [3], citing Mearns et al., 2015 [4], and Kashiwagi et al., 2014 [5], has shown that this class is composed by the following drugs: canagliflozin, dapagliflozin, empagliflozin, and new drugs were approved to clinical usage, which are ipragliflozin, tofogliflozin and luseogliflozin.

One of the most important vantages of the class, compared to other hypoglycemic substances, is that the long-term use does not cause impaired treatment efficacy, due to incapacity to cause damages to beta pancreatic cells [6].

The combination of SGLT2 inhibitors with other drugs has shown addictive effects in the enhancement of glucose metabolism, compared to other isolated oral anti-diabetic substances [7].

Tjerk et al., 2016 [8], highlighting the knowledge of Bailey et al., 2010 [9], and Bell et al., 2016 [10], demonstrate that the association between dapagliflozin and metformin (Biguanide) has synergic effects in the glucose metabolism in kidneys and liver, thus it is recommended by FDC. A new medication composed by the combination of these drugs was recently approved (Dapagliflozin 2,5mg/metformin 850mg or dapagliflozin 5mg/metformin 1000mg), leading to a greater treatment adherence, once it diminishes the quantity of pills ingested per day. Nevertheless, the combination is therapeutically equivalent to those separately administrated individual components.

The association of Empogliflozin and Linagliptin (DPP4 inhibitor) had greater effect in the reduction of glycated hemoglobin (HbA1C) and triglycerides (TGs), and, also, addictive effect as enhancer of glucose metabolism, compared to monotherapy. There was significant improvement of insulin sensibility, which led to a greater management of glucose levels in the insulin resistant states [7].

In patient with refractory type 2 diabetes using metformin and vidagliptin, the association with dapagliflozin and a diet with carbohydrate 128g/day, without total caloric restriction, demonstrated better management of postprandial glycaemia, without augment in insulin secretion [11].

The final concentration of metformin was reduced after the alimentation, independently of the caloric content, compared to final concentration of dapagliflozin, without alteration in action mechanism [8].

Evidences show that the association of diuretics and luseogliflozin has shown better results, compared to the isolated use of these drugs, in patient with metabolic syndrome [12].

The weight loss after 5 weeks of treatment, the reduction in triglycerides level, the reduction of post-prandial glycaemia and the reduction of arterial pressure in type 2 diabetic patients, due to the augment in sodium urinary excretion, are the main effects of these associations. However, they did not influence the fasting glycaemia and did not alter the total cholesterol and free fatty acids levels [12].

The association of canagliflozin, DPP4 inhibitors and GLP1 agonists also has demonstrated reduction of HbA1C levels to values inferior than 7%, reduction of systolic arterial pressure and weight loss, compared to placebo. However, the consequences to reduce lipid levels were inconclusive, differently of some past studies [13].

Given what was discussed, a promising action of the SGLT2 inhibitors, in its isolated effect and in the association with other hypoglycemic substances, is being revealed, once its action mechanism has shown great efficacy to treat Diabetes Mellitus in any stage of this disease, obtaining great results in glycated hemoglobin and glycaemia control.

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