EFFECTS OF SGLT2 INHIBITORS ON CARDIAC FUNCTION IN CHRONIC HEART FAILURE

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Abstract: *Many clinical studies have explored sodium–glucose cotransporter 2 (SGLT2) inhibitors in patients with chronic heart failure (CHF), with or without type 2 diabetes mellitus and SGLT2 inhibitors were proved to significantly reduce CHF hospitalization, cardiovascular death, cardiovascular mortality, all-cause mortality and myocardial infarction in patients with or without type 2 diabetes. However, only a limited few have investigated the effects of SGLT-2 inhibitors on HF disease-specific health status and cardiac function. This article describes to assess the effects of SGLT2 inhibitors on cardiac function in CHF patients.*

Key words: *SGLT2 inhibitors, chronic heart failure, type 2 diabetes.*

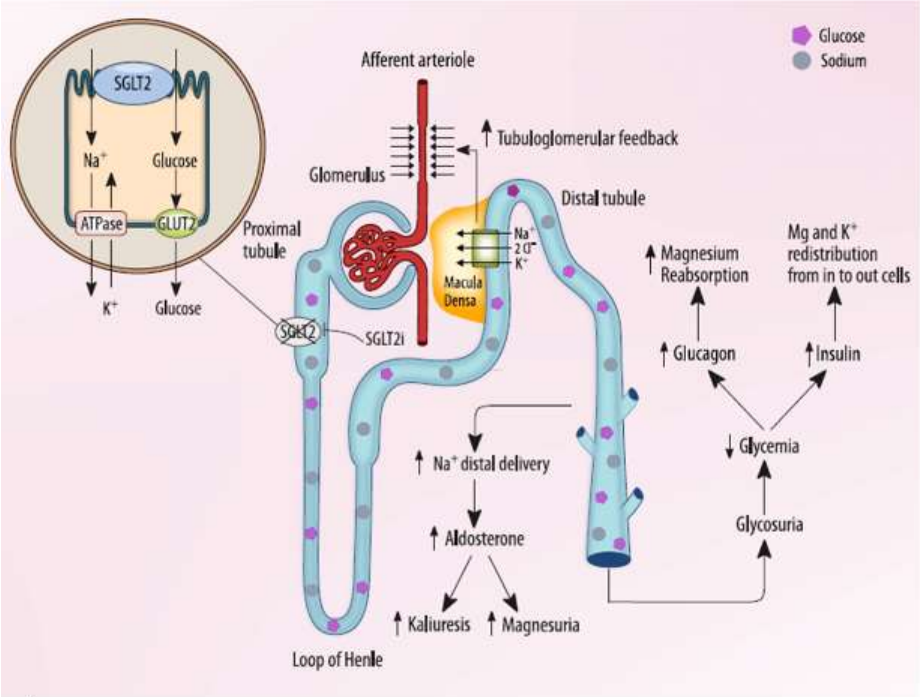
INTRODUCTION

Chronic heart failure (CHF) is a terminal state of various heart diseases, with high morbidity, hospitalization rate and fatality rate. Based on the left ventricular ejection fraction (LVEF), CHF can be categorized into heart failure with reduced ejection fraction (HFrEF, LVEF ‹ 40%), heart failure with preserved ejection fraction (HFpEF, LVEF ≥ 50%), and heart failure with mildly reduced ejection fraction (HFmrEF,40% ≤ LVEF ‹ 50%). In Uzbekistan, heart failure remains the leading cause of hospitalization. Drug therapy is an important and critical measure to improve the quality of life and prolong the survival of patients with CHF. The conventional medical treatment for CHF, often referred to as the "golden triangle", includes angiotensin-converting enzyme inhibitors /angiotensin II receptor antagonists, β-blockers, and mineralocorticoid receptor antagonists.

In recent landmark clinical trials, sodium-glucose co-transporter 2 (SGLT2) inhibitor therapies improve blood glucose control and also reduce cardiovascular events and heart failure hospitalizations in patients with type 2 diabetes.

Sodium glucose co-transporter 2 (SGLT2) inhibitors were originally developed to treat hyperglycemia in patients with type 2 diabetes and became further a cornerstone of treating patients with chronic heart failure (CHF). The precise mechanisms of the cardiovascular protective properties of SGLT2 inhibitors are only partially understood.

In updated guidelines, SGLT2 inhibitors (dapagliflozin, empagliflozin and sotagliflozin) are strongly recommended for reducing cardiovascular death and heart failure hospitalization in patients with HFrEF (class I). However, recommendations for SGLT2is in HFpEF and HFmrEF are either absent or less robust (class II). We can understand mechanism of SGLT2 inhibitors in picture-1.



Picture-1. Picture was taken from mavink.com website.

The carrier for Na-glucose cotransport is located in the luminal membrane of intestinal mucosal and renal proximal tubule cells. After filtration some of glucose cross the membrane of glomerular capillaries, however not all of them. This part of filtrated glucose must reabsorb, so SGLT 2 channels reabsorb it. Glucose is transported "uphill"; sodium is transported "downhill." Energy is derived from the "downhill" movement of sodium. The inwardly directed sodium gradient is maintained by the Na-K pump on the basolateral (blood side) membrane. Poisoning the Na-K pump decreases the transmembrane sodium gradient and consequently inhibits Na-glucose cotransport. When sodium and glucose cross membrane they pull water. After that much water is reabsorbed and volume of water is increased in the serum. Arterial blood pressure depends on volume of blood too, so it is increased. Growing volume of blood in veins increases preload of heart. So, we achieve via decreasing water volume of serum cardiac preload of patient who suffered from chronic heart failure. However, SGLT 2 inhibitors make excretion more sodium and glucose in the urine.

Materials and methods

An extensive search for clinical trials in PubMed, EMBASE, CENTRAL, Scopus, ESC were also searched for the terms “SGLT2 inhibitor”, “sodium glucose cotransporter 2 inhibitor”, “gliflozin”, “dapagliflozin”, “canagliflozin”, “empagliflozin”, “ipragliflozin”, “sergliflozin”, “sotagliflozin” was performed. The search strategy was adapted for each of the databases, and references of included studies were also reviewed.

Result

Weight loss from SGLT2-inhibitor therapy occurs due to an increased glucagon:insulin ratio causing increased lipid mobilization and is thought to be one of the mechanisms involved in reduction in heart failure mortality associated with SGLT2-inhibitor therapy on the other hand this therapy is associated with increases in renal erythropoietin production, red blood cell mass and hematocrit. Cardiac hypertrophy,

fibrosis and inflammation lead to adverse cardiac remodeling in heart failure, and this is a key contributor to its severity. Some pre-clinical and clinical studies have demonstrated a role for SGLT2-inhibitor therapies in reversing adverse cardiac remodeling. Although this effect has been observed in patients with type 2 diabetes and left ventricular hypertrophy, it has not been seen in patients with heart failure. This is intriguing, particularly, since the majority of its cardiovascular benefits have been around heart failure outcomes. This raises the possibility that, in the context of heart failure, SGLT2 inhibition may have novel direct cardioprotective effects, beyond that of ventricular loading and remodeling.

SGLT2-inhibitor therapy increases hepatic synthesis and decreases the urinary excretion of ketones producing a mild and persistent state of hyperketonemia. cardiovascular benefits of SGLT2-inhibitor therapy may be related to a shift in cardiac metabolism away from fatty acids and glucose oxidation towards more oxygen-efficient ketone bodies, thereby improving cardiac efficiency.

These findings suggest that altered myocardial calcium handling is involved in the development of cardiac hypertrophy and heart failure, and that SGLT2-inhibitor therapy may improve the electrochemical characteristics in the failing myocardium which may contribute to its cardiovascular benefit.

Conclusion

SGLT2-inhibitor therapies are a promising new class of drugs for treating type 2 diabetes and chronic heart failure. The cardioprotective effect of SGLT2 inhibition has been demonstrated in morphological changes in the myocardium and type 2 diabetes with chronic heart failure.

LITERATURE:

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