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Impact of SGLT2 inhibitors treatment on the chronic kidney disease in people with type 2 diabetes

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Abstract

Diabetes is the most common cause of CKD (chronic kidney disease). CKD is also one of the most important diabetic complication. SGLT2 (sodium glucose co-transporter-2) inhibitors are new class of medication used to lower high blood glucose level in people with type 2 diabetes. In new researches SGLT2 inhibitors demonstrated a significant and clinically relevant reduction in the risks of albuminuria and progression of nephropathy, doubling of

serum creatinine levels, and initiation of renal replacement therapy. This review focuses on the therapeutic effectiveness of using SGLT2 inhibitors for the treatment of CKD in type 2 diabetes.

Keywords: SGLT2, sodium glucose co-transporter-2 inhibitors, type 2 diabetes, chronic kidney disease

Introduction

Chronic kidney disease (CKD) has become a global public health issue in recent years due to its high prevalence, low awareness, low treatment, and low control rates [1, 2]. Diabetes is a frequently occurring and common disease in the world. It is estimated that more than 400 million people will have diabetes by 2030 [3]. Two large clinical trials clearly indicated that intensive glycemic control slows the progression of diabetic complications, including diabetic kidney disease (DKD). These clinical studies suggest that hyperglycemia is a major factor in developing DKD. [4,5] Patients with CKD and type 2 diabetes mellitus (T2DM) require also more comprehensive management, including the control of urinary protein levels. Albuminuria and microalbuminuria can significantly increase CKD progression and the incidence of cardiovascular complications. [6] The emergence of sodium-glucose co-transporter (SGLT)-2 inhibitors provides a new direction for the treatment of patients with chronic renal disease complicated by diabetes. [7] They inhibit SGLT-2 proteins which are found mainly in the kidneys and are responsible for about 90% of the reabsorption of glucose. SGLT2 inhibitors also accords other benefits, such as weight loss, low incidence of hypoglycemia, and reduction in blood pressure. [8,9]

Aim of the study

The aim of the study is to statistical data the literature and present the current state of the therapeutic effectiveness of using SGLT2 inhibitors for the treatment of CKD in type 2 diabetes.

Material and method

The method of study is descriptive epidemiological analysis. Information that has been used is derived from statistical data provided by the WHO. In searching for them on the WHO, PubMed website and Google Scholar, keywords such as: SGLT2, sodium glucose co-transporter-2 inhibitors, type 2 diabetes, chronic kidney disease.

Results

The are a few studies on the effect of SGLT2 inhibitors, which has shown significant beneficial effects on people with CKD and type 2 diabetes.

A group of patients with CKD entered randomisation were half of them where treated with placebo and another half with SGLT2 inhibitors. Patients receiving empagliflozin showed lower HbA1c and significant reductions in bodyweight, systolic blood pressure, diastolic blood pressure at the end of trail compared with placebo, without increases in pulse rate (figure 1). [10] In another study researchers tested luseogliflozin and results where similar. It shows decrease of HbA1c, FPG (fasting plasma glucose), blood pressure and body weight in 24-week. In addition they confirmed that the higher the baseline HbA1c, the greater the decrease in HbA1c across all eGFR groups. [11]

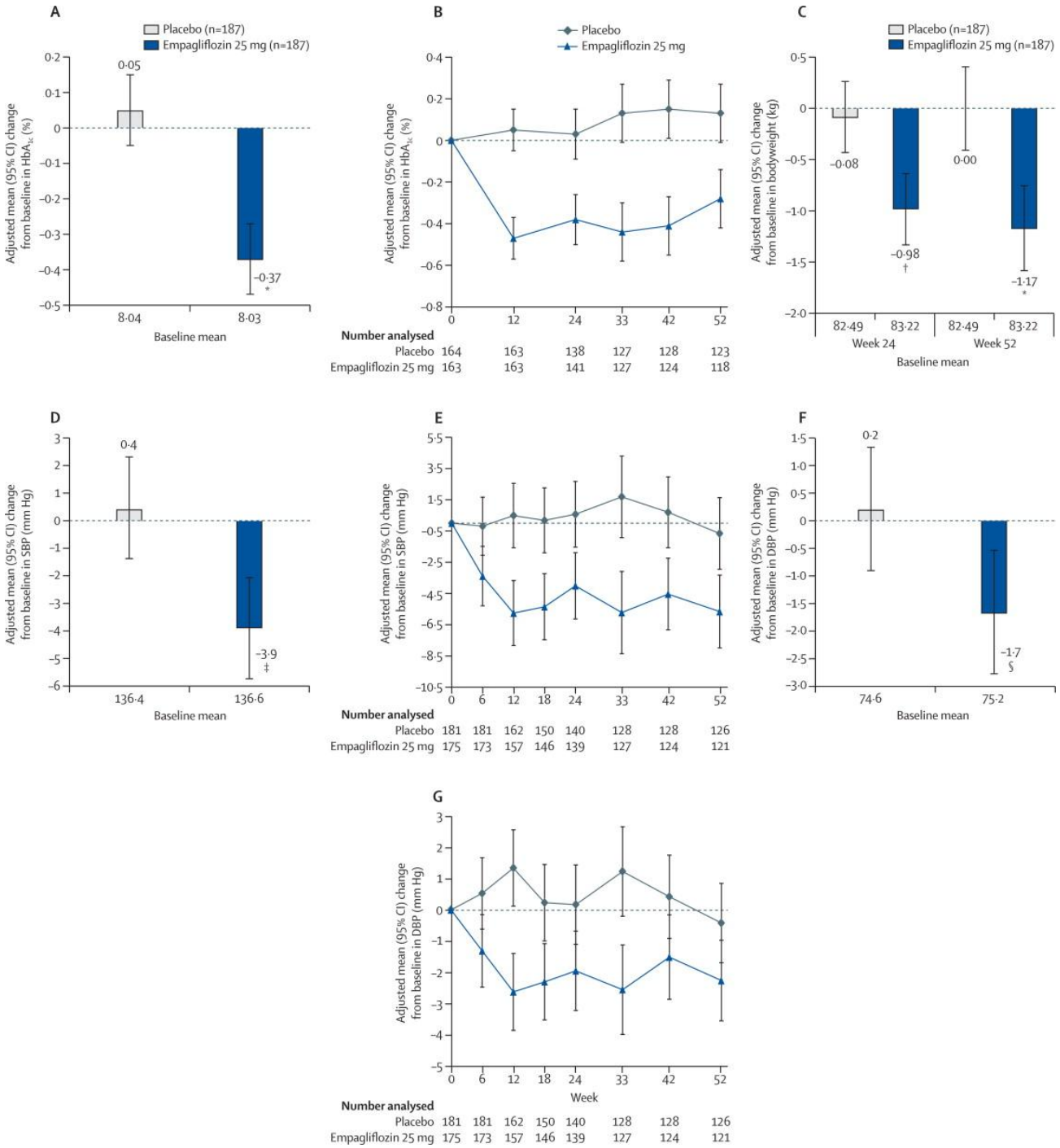

Figure 1: efficacy in patients with stage 3 CKD

Small decreases in eGFR were noted in the empagliflozin groups, which returned to baseline after few weeks (figure 2). More patients improved from macroalbuminuria at baseline to microalbuminuria, or from or microalbuminuria to no albuminuria, at end of treatment. [10] Using luseogliflozin urinary albumin was not significantly different, although it tended to decrease especially in those with moderate renal impairment whose baseline value was higher. [11]

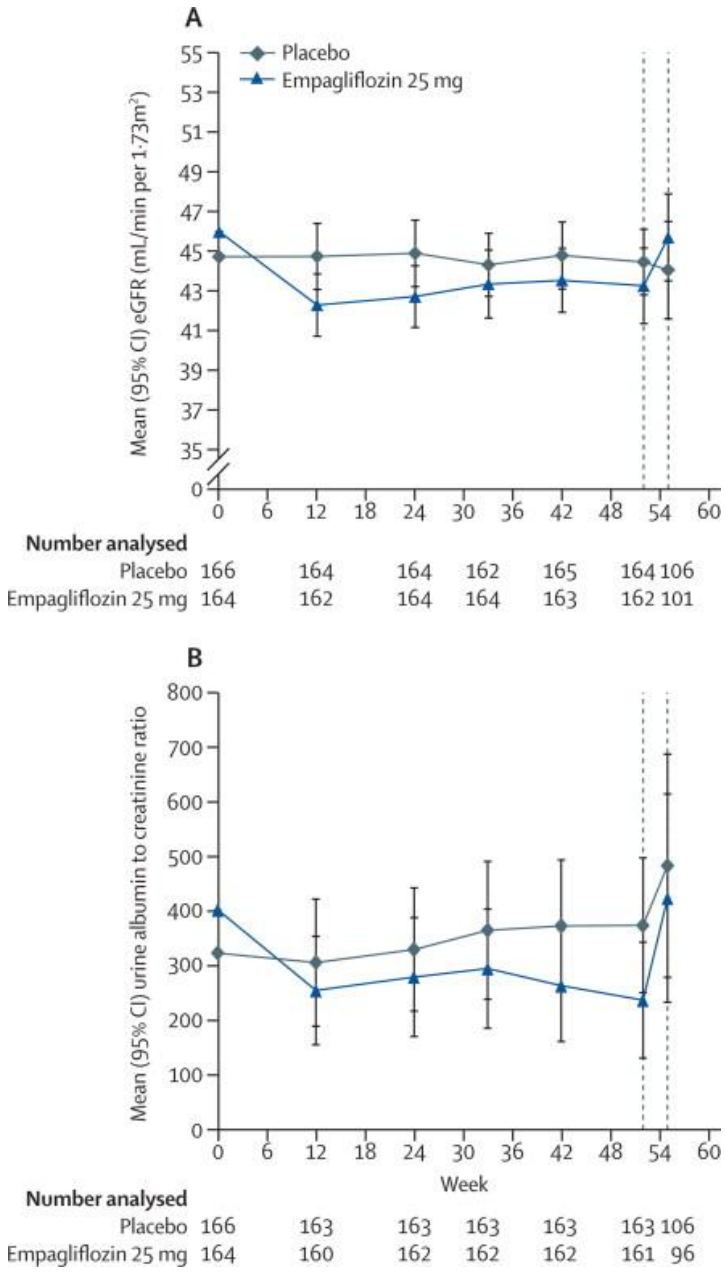

Figure 2: eGFR and urine albumin to creatinine ratio in the full analysis set of patients with stage 3 CKD who completed 52 weeks of treatment

In addition to above-mentioned benefits, some SGLT2 inhibitors can have extra effects. Dapagliflozin for example was associated with fewer episodes of, and fewer discontinuations for, hyperkalemia compared with placebo. [12]

In comparison to other types of medication, SGLT2 inhibitors use was associated with a lower risk of composite kidney outcomes and a lower incidence of ESKD (end-stage kidney disease) than GLP1RA use. [13]

Discussion

Diabetes is one of the most common diseases in 21st century with increasing number of people affected. It has many complication including chronic kidney disease. Renal dysfunction affects not only kidneys but whole patient body. SGLT2 Inhibitors are promising new group of medication used for controlling the course of type 2 diabetes and it's symptoms. As written earlier hyperglycemia is a major factor in developing DKD. Researches show that SGLT2 Inhibitors reduce HbA1c and FPG [14]. Better glucose control leads to less complication.

SGLT2 inhibitors can modulate activation of the tubulo-glomerular feedback through an increase in sodium delivery to the macula densa. The result is a reduction in the vasodilation of afferent arterioles and, in turn, reductions in glomerular hypertension and subsequent albuminuria with beneficial effects on the progression of renal damage. Hyperfiltration is indeed a one of the major determinant of CKD progression modulated by SGLT2i [15]

Proteinuria is another risk factor and research has shown that positive urine protein at baseline is associated with a significantly increased risk of developing CKD. [16] Persistent albuminuria induces inflammation and chemokine secretions in the proximal tubules, and it finally accelerates fibrosis. [17]. Using SGLT2 inhibitors reduce albuminuria and can slow progression of CKD especially in people with higher baseline UACR (Urine Albumin-Creatinine Ratio) [16]

Reduction in blood pressure, body weight, increased uric acid excretion, and change in fuel metabolites have also been suggested to kidney protective effects. [18]

Using a SGLT2 inhibitor shows a major benefit on renal outcome, but also on heart failure and major adverse cardiovascular events in people with type 2 diabetes, urine albumin creatinine ratio >300 mg/g and eGFR 30-90 ml/min/1.73m2. [19]

Conclusions

1. SGLT2 Inhibitors lower HbA1c and fasted plasma glucose in patients with diabetic kidney disease.

2. SGLT2 Inhibitors reduce albuminuria and glomerular hypertension which can slow progression of CKD.

3. Patients in addition showed significant reductions in bodyweight, systolic and diastolic blood pressure without increasing heart rate.

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