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TREATMENT OF TYPE-2 DIABETES MELLITUS WITH SGLT-2 INHIBITORS AND INFLUENCE ON RENAL FUNCTION

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ABSTRACT

Type 2 diabetes is a global problem with increasing incidence. Globally, more than one in 10 adults are now living with diabetes. It is the leading cause of chronic kidney disease (CKD) worldwide and its incidence continues to rise. CKD is associated with progressive loss of kidney function. Early stages of CKD may be reversible. Therapeutic control of diabetes is more difficult in patients with renal impairment, requiring a therapeutic approach with increased caution. There are advances in available glucose-lowering agents for the treatment of type 2 diabetes that not only modify the disease itself, but also have important benefits in terms of associated cardiovascular risk factors. Sodium glucose cotransporter 2 (SGLT2) inhibitors have demonstrated significant benefits in reducing major adverse cardiovascular events, heart failure hospitalization, mortality, plus the renoprotective benefit they provide.

KEYWORDS: diabetes type 2, SGLT 2 inhibitors, renal function.

INTRODUCTION

The number of patients with diabetes is projected to increase from ~450 million in 2017 to over 690 million in 2045.[1] Diabetic nephropathy occurs in 20-40% of patients with DM and is an independent and leading cause of chronic renal failure.[2] Diabetes mellitus (42%), hypertension (18%) and glomerulonephritis (18%) are the main causes of CKD.[3]

Globally, ~700 million people have CKD.[4]

Within the next 10 years, a dramatic increase in CKD-related morbidity and the need for kidney transplantation is expected.[5] People with CKD are 5-10 times more likely to die prematurely than to progress to TBN. According to WHO data, CKD is expected to become the 5th cause of death in the world by 2040.

CKD-associated mortality is increasing.[6] CKD is an important risk factor for premature death and cardiovascular complications, incl. HF.[7]

As eGFR decreases and the degree of albuminuria increases, the risk of HF, nonfatal MI, and death increases.[8]

Chronic kidney disease (CKD) is usually a long-term, asymptomatic disorder that develops slowly at first and often goes unnoticed until an advanced stage occurs. Early protection and prevention are of key importance in CKD, as is its early diagnosis. Screening is extremely important for early diagnosis and optimal disease control.[9]

Identifying and addressing risk factors such as high blood pressure, diabetes, smoking and obesity is essential. These risk factors greatly increase the likelihood of developing CKD, so controlling them can help control the risk.[10]

Kidney health is also closely related to the health of the cardiovascular and metabolic systems.[11]

Many of the risk factors that can increase the likelihood of developing CKD are the same risk factors that can increase the risk of developing type 2 diabetes mellitus (T2DM) or cardiovascular (CVD) disease. Providing protection for one of these diseases may also provide protection from the other diseases.[12]

Lifestyle changes, such as controlling blood pressure, maintaining a healthy weight, following a kidney-friendly diet, and timely treatment of CKD with nephroprotective drugs, can have an important beneficial effect and slow its progression.[13]

In recent years, the therapeutic class of inhibitors of the sodium-glucose cotransporter 2 (SGLT2 inhibitors) has distinguished itself with many positive effects in the treatment of diseases from the spectrum of cardio-renal-metabolic disorders, namely: diabetes mellitus type 2, chronic heart failure (CH) and chronic kidney disease. Two of the representatives of

the therapeutic class in Europe are indicated for the treatment of each of the three diseases - dapagliflozin and empagliflozin.

In parallel with the accumulating data from randomized clinical trials showing complex cardio-renal-metabolic benefits of some modern drugs, the therapeutic guidelines for the treatment of T2DM, for the control of chronic heart failure and for the therapy of chronic kidney disease have been substantially changed.[14]

MATHERIALS AND METHODS

The aim of the present study was to analyze and evaluate how SGLT-2 inhibitor treatment affects renal function in patients with type 2 diabetes mellitus. The survey was conducted in the period of November 2022. – July 2023 in the Burgas region of the Republic of Bulgaria.

Participants are randomly selected based on the following inclusion criteria:
- age over 18 years;
-diagnosis of DM type 2 with a prescription of at least 6 months
- treatment with metformin and/or SUP before inclusion in the study
- voluntary consent to participate

Patients meeting the following exclusion criteria were not included:
- DM type 1;
- gestational diabetes mellitus;
- age under 18 years;
- patients with cognitive disorders and mental illnesses

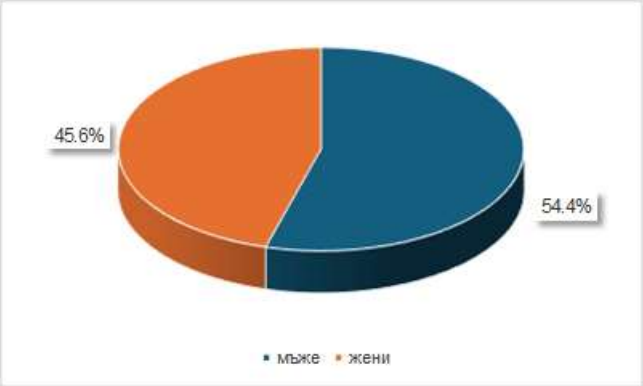
The sources for collecting information are outpatient lists, epicrisis, laboratory tests. The study group included 57 patients with type 2 diabetes mellitus on metformin and/or SUP treatment, in whom we started treatment with an SGLT-2 inhibitor. Metabolic control parameters that we tracked at the beginning and end of the six-month follow-up period were creatinine, calculated glomerular filtration using the CKD-EPI method (Equations for Glomerular Filtration RATE)

The statistical method used is the Independent Samples T-test. With this test, the statistically significant differences between the average values of the indicators with a high degree of statistical significance (Sig. (2-tailed) $<\alpha=0.05$) are established.

Sig (p) represents level of significance, probability with which the 0th hypothesis is accepted, t-compares two mean values - Student's t-test - hypothesis analysis. The implementation was carried out with the statistical package SPSS 22.

RESULTS AND DISCUSSION

Out of a total of 57 patients treated with an SGLT-2 inhibitor, 31 (54.4%) were men and 26 (45.6%) were women.



Male-45.6% Female-54.4%

Fig. 1: Distribution of patients by gender who took the medication SGLT-2.

The mean age of the patients taking the SGLT-2 inhibitor medication was 60.33±9.44 years.

Table 1: Change in paraclinical parameters of patients taking SGLT-2 inhibitors.

	period	mean	Statistical significance
Glomerular filtration(ml/min)	baseline	79.47±18.13	p≥0.05
	after 6 months	85.58±19.03	
creatinine (mcmol/l)	baseline	86.59±18.12	p≥0.05
	after 6 months	79.86±19.53	

Independent Samples T-Test shows that the difference between the mean values of creatinine at the beginning of the study and after 6 months, which amounts to 6.730 mcmol/l is not statistically significant, as characteristics t = 1.874 is with significance level Sig. = 0.064> α = 0.05.

The difference between the mean values of glomerular filtration at the beginning of the study and after 6 months, which was 6.721 ml/min, was not statistically significant, as the significance level of characteristics t = -1.442 has significance levels Sig. = 0.087> α = 0.05.

Despite the lack of statistical significance in the improvement of GF and the reduction of serum creatinine after 6 months of treatment with an SGLT-2 inhibitor, the data from the analysis are indicative of the positive effect that these medications have on renal function.

The lack of statistically significant improvement in the above indicators is probably due to the short 6-month period of treatment with SGLT-2 inhibitors after which we analyzed the data.

The emergence of new medicinal products for the treatment of type 2 DM in recent years is increasingly displacing the traditional conventional treatment with metformin and SUP.

According to the 2021 ADA/EASD consensus report on the treatment of type 2 diabetes mellitus, glucose-lowering therapy focuses on GLP-1 receptor agonists and SGLT-2 inhibitors, taking into account some clinically relevant factors. Treatment with GLP-1 receptor agonists is recommended in patients with diabetes mellitus with established cardiovascular disease or at high risk for such disease.

In patients with chronic kidney disease and heart failure, treatment with SGLT-2 inhibitors is recommended, given the beneficial effects in terms of reducing the progression of CKD, the nephroprotective effect and hospitalizations for HF.

CONCLUSION

A careful therapeutic approach is required for patients with chronic kidney disease and T2DM. There should be increased control of risk factors beyond blood glucose and HbA1c control.

The modern concept is that the therapy of patients with ZDT2 is shifted beyond the glycemic effect of SGLT2i and an opportunity is given for complex treatment and stopping the development of. Given the additional protection they provide, SGLT2-inhibitors should be considered as a mainstay in the treatment of T2DM.The short follow-up period of the patients and the limited sample from only one region of Bulgaria can be pointed out as the main drawback of the study.

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