
Original article

The Role of SGLT2 Inhibitors In the Complex Treatment of Patients with CKD – The Results of one Tertiary Center

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Abstract

Introduction. Chronic kidney disease (CKD) represents a major and increasing social and economic problem, as it affects between 6 and 18% of the population worldwide and is associated with a high cardiovascular risk, morbidity and mortality. SGLT2-inhibitors have central role in the complex treatment of patients with CKD of different etiology, as first-line nephroprotective agents both in patients with and without concomitant or underlying diabetes mellitus. The aim of our study was to evaluate the effects of two commercially available SGLT2-inhibitors (dapagliflozine and empagliflozine) on renal parameters in patients with CKD and biopsy-proven glomerular diseases at the background of standard treatment in a real-life observational study.

Methods. In 2024 we observed 54 CKD patients (33 males, aged 19-85 years) treated with SGLT2-inhibitors (dapagliflozine and empagliflozine registered for standard-of-care treatment of CKD in our country) for 6 months, at the background of standard treatment for the underlying disease. All patients had CKD, with biopsy-proven renal disease: 20 had diabetic nephropathy at the background of type 2 diabetes mellitus (DM2), 4 had systemic amyloidosis with renal involvement (2 had AA and 1 had AL type), 20 had biopsy-proven glomerulonephritis, and 10 had hypertensive nephropathy. Three of the patients with glomerulonephritis had concomitant DM2. Overall, 38 received dapagliflozine and 16 were on empagliflozine. All patients were followed for 3 months and 32/54 were followed until month 6. The patients were evaluated at the initiation of the treatment and at 3 and 6 months. All patients received standard-of-care treatment for the renal and accompanying diseases. Written informed consent was obtained from all patients prior to any medical procedures.

Results. During the follow-up we observed stabilization of renal function with no significant changes in serum creatinine and eGFR, a decrease in serum uric

acid levels and proteinuria, with no significant side effects. These effects showed no differences between male and female patients and across the different disease entities.

Conclusion. The results of our study are confirmatory in nature and support the use of SGLT2-inhibitors as nephroprotective agents and across various CKD entities.

Keywords: chronic kidney disease, SGLT2-inhibitors, nephroprotection, diabetes, glomerulonephritis, hypertensive nephropathy, uric acid, proteinuria

Introduction

Chronic kidney disease (CKD) is defined as presence of kidney damage (based on laboratory, imaging or histopathological data) or an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m² or markers of kidney damage (albuminuria, pathological urinary sediment, abnormal imaging results, tubular disorders, or a history of kidney transplantation), persisting for at least 3 months, irrespective of the cause [1]. CKD represents a major and increasing social and economic problem, as it affects between 6 and 18% of the population worldwide and is associated with high cardiovascular risk, morbidity and mortality [2]. SGLT2-inhibitors have central role in the complex treatment of patients with CKD of different etiology, as first-line nephroprotective agents both in patients with and without concomitant or underlying diabetes mellitus [3,4]. The aim of our study was to evaluate the effects of SGLT2-inhibitors on renal parameters in patients with CKD and biopsy-proven glomerular diseases at the background of standard treatment in a real-life observational study, first one at our institution.

Materials and methods

In 2024 we observed 54 CKD patients treated with two available SGLT2-inhibitors (dapagliflozine and empa-

gliflozine registered for standard-of-care treatment of CKD in our country), at the background of standard treatment for the underlying disease, for a period of 6 months. Our group consisted of 54 patients (33 males, aged 19-85 years). All patients had CKD [1,2], with biopsy-proven renal disease: 20 had diabetic nephropathy at the background of type 2 diabetes mellitus (DM2), 4 had systemic amyloidosis with renal involvement (2 had AA and 1 had AL type), 20 had biopsy-proven glomerulonephritis (GN) [6-IgA GN, 5-focal and segmental glomerulosclerosis (FSGS), 5-systemic lupus erythematosus (SLE) with lupus nephritis (LN), 2-mesangioproliferative GN, 1-primary membranous GN (MGN), 1-polyangiitis with granulomatosis, and 10 had hypertensive nephropathy]. Three of the patients with glomerulonephritis had concomitant DM2. Overall, 38 received dapagliflozine and 16 were on empagliflozine. All patients were followed for 3 months and 32/54 were followed until month 6. The patients were evaluated at the initiation of the treatment and at 3 and 6 months. All patients received ACE-inhibitor or AT2-blocker, all patients with GN received pathogenetic treatment, according to the standard treatment protocols, amyloidosis patients received also colchicine treatment. None of the diabetic patients was on insulin treatment, and they received standard-of-care treatment for DM2, in accordance with the accepted Good Clinical Practice guidelines in Bulgaria [5]. Following parameters were evaluated, using standard methods: hemogram (complete blood count), biochemical investigations of the blood (creatinine, urea, uric acid, lipidogram, fasting blood glucose, potassium, sodium, chlorides, calcium, phosphates, liver enzymes (ASAT, ALAT, GGT, Alkaline phosphatase), total protein and serum albumin levels), urine investigations (proteinuria, urinalysis, if needed-microbiological investigation of the urine), estimated glomerular filtration rate (eGFR, according to the MDRD formula [6]). The statistical analysis was performed using a standard SPSS 27 pack for Windows. Written informed consent was obtained from all patients prior to any medical procedures.

Results

There was stabilization of serum creatinine and eGFR (Figure 1), decrease in proteinuria (Figure 2), and reduction in uric acid levels (Figure 3) in the majority of patients (Table 1). A sole statistically significant difference

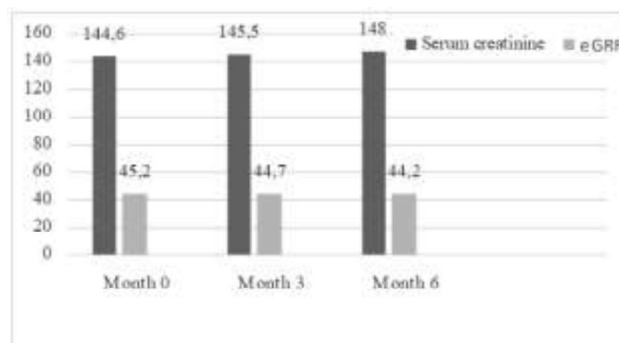


Figure 1. Changes in the mean serum creatinine (μmol/L) and eGFR (ml/min/1.73 m², calculated according using the MDRD formula) during the 6 months treatment. p=NS for all comparisons

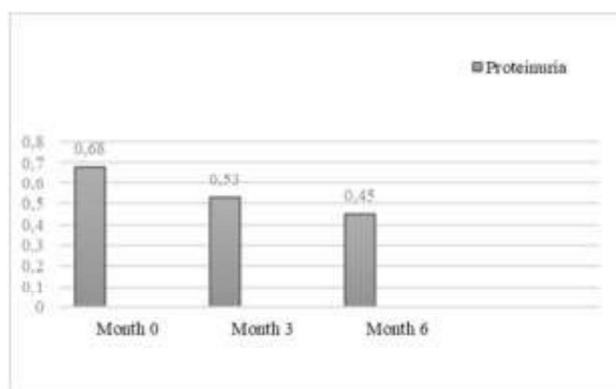


Fig. 2. Changes in the mean levels of proteinuria (g/L) during the 6 months treatment. p=NS for all comparisons

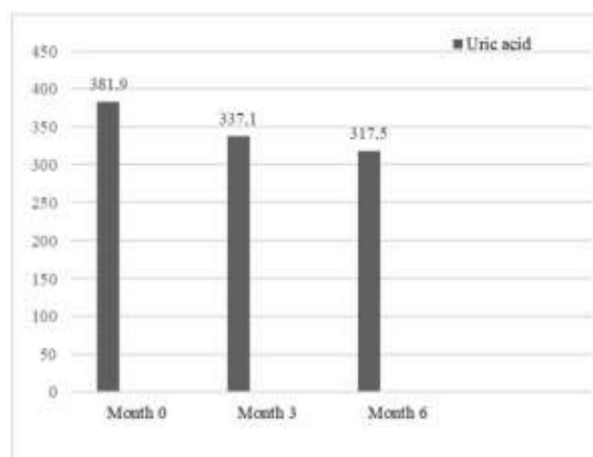


Fig. 3. Changes in the mean serum uric acid levels (μmol/L) during the 6 months of treatment. For comparisons at month 0 vs month 3 and 6 - p<0.05; for comparison at month 3 vs month 6 p=NS (>0.05)

Table 1. Changes in mean levels of serum creatinine (mcmol/l), GFR (ml/min/1.73 m², calculated using the MDRD formula), uric acid (μmol/L) and proteinuria (g/L) during the 6-months treatment (p<0.05 for changes in uric acid levels – month 0 vs month 3 and 6; p=NS for the rest).

Months	Serum creatinine (μmol/L)	eGFR (ml/min/1.73 m ²)	Serum uric acid (μmol/L)	Proteinuria (g/L)
0 (54 patients)	144.6 +/- 56.7	45.2 +/- 20	381.9 +/- 121.3	0.68 +/- 1.5
3 (54 patients)	145.5 +/- 58.8	44.7 +/- 20.4	337.1 +/- 82	0.53 +/- 1.2
6 (32 patients)	148 +/- 59.6	44.2 +/- 20.4	317.5 +/- 79.2	0.45 +/- 1.1

rence was observed between the levels of the uric acid at months 0 and 3, and months 0 and 6 (figure 3), without a statistically significant difference between months 3 and 6 (figure 3). There were no changes in hemogram, serum electrolytes, calcium and phosphate levels, total protein and serum albumin levels, blood glucose and liver enzymes levels during the follow-up. Only 3 patients developed lower-urinary-tract infections that did not lead to discontinuation of the treatment. We observed no cases of hypoglycemia, ketoacidosis or significant worsening of renal function. There was no treatment discontinuation in any of the patients. We found no difference in the effect of both SGLT2-inhibitors in men and women and across different disease entities.

Discussion

SGLT2-inhibitors are one of the widely accepted nephro-protective strategies both in patients with diabetic and non-diabetic CKD [3]. They have beneficial effect on renal function, proteinuria and uric acid levels mediated via their hypoglycemic, hemodynamic and pleiotropic effects, including effects on glomerular structures and endothelial cells [3,4].

The results of our observational study confirm the beneficial effects of two SGLT2-inhibitors in patients with CKD of different etiology (both diabetic and non-diabetic) with statistically significant decrease of uric acid levels. The reduction in proteinuria did not reach significant level and the creatinine and GFR were stabilized. There were no side effects detected.

Our study included a small number of CKD patients that were followed up for only 6 months. Therefore, two major limitations in our study were the small cohort and short observational period. Nevertheless, our results revealed a stabilization of renal function, i.e. a decrease in the rate of renal function loss, with a decrease of both hyperuricemia and urine protein loss. Further studies in larger cohorts and longer observation periods are needed for the validation of these results.

Conclusion

In conclusion, the results of our small study in patients with CKD with different etiology and biopsy-proven glomerular involvement, revealed the beneficial effects of the two commercially available SGLT2-inhibitors used for nephroprotection-stabilization of renal functional parameters and decrease in serum uric acid levels and proteinuria, two well-known risk factors for progression of both CKD and cardio-vascular complications. The absence of significant side effects of treatment and our results are in favor of the use of these medications in patients with CKD of different origin. This was an investigator-driven study and has no commercial support. The authors have no conflicts of interest, associated with this study. The results of the current study were presented as electronic poster at the CaReMeLO 2025 Conference, Warsaw, Poland, 30-31 May, 2025.

Conflict of interest statement. None declared.

References

1. Vaidya SR, Aeddula NR. Chronic Kidney Disease. In: *StatPearls* <https://www.ncbi.nlm.nih.gov/books/NBK535404/>.
2. Chen TK, Knicely DH, Grams ME. Chronic Kidney Disease Diagnosis and Management: A Review. *JAMA* 2019; 322(13): 1294-1304.
3. Gajewska A, Wasiak J, Sapeda N, *et al.* SGLT2 Inhibitors in Kidney Diseases-A Narrative Review. *Int J Mol Sci* 2024; 25(9): 4959.
4. Granata A, Pesce F, Iacoviello M, *et al.* SGLT2 Inhibitors: A Broad Impact Therapeutic Option for the Nephrologist. *Front Nephrol* 2022; 2: 867075.
5. Recommendations for good clinical practice for the treatment of diabetes mellitus. Bulgarian society of endocrinology, 2019, Accessible at: <https://endo-bg.com/wp-content/uploads/2019/10/endo-zaharen-diabet-2019.pdf>.
6. Levey AS. A More Accurate Method To Estimate Glomerular Filtration Rate from Serum Creatinine: A New Prediction Equation. *Ann Intern Med* 1999; 130: 461-470.