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Short-Term Effect of Sodium Glucose Co–Transporter 2 Inhibitors on Routine Laboratory Examinations

SGLT-2 İnhibitörleri'nin Kısa Vadede Bazı Laboratuvar Testleri Üzerine Etkisi

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Abstract

Background: In this study, we aimed to examine the effect of Sodium Glucose Cotransporter 2 inhibitors (SGLT-2i) on routine laboratory test results at 12 weeks of follow-up among type 2 diabetes mellitus (T2DM) patients using empagliflozin and dapagliflozin.

Material and Method: Three hundred ten patients with a diagnosis of T2DM (over 18 years of age) with SGLT-2i added to stable triple combination therapy were included in this study. Patients who received either empagliflozin (10 mg once daily) (n:170) or dapagliflozin (10 mg once daily) (n:140) in addition to their current treatment regimen were divided into two groups. Laboratory findings of all patients were recorded before treatment and during follow-up in the 12 weeks.

Results: Both empagliflozin and dapagliflozin had similar profiles of improvement of mean fasting blood glucose, and HbA1c. High improvement in lipid profiles and spot urinary parameters were detected in dapagliflozin group compared to empagliflozin group. At 12-week follow-up, change in other laboratory parameters did not differ significantly between the groups. In terms of total side effects, no difference was observed between treatment groups.

Conclusions: Empagliflozin and dapagliflozin had similar effects on fasting blood glucose and HbA1C at 12-week follow-up. It can be considered that dapagliflozin may be preferred due to its positive effect on the lipid profile, especially in the population with cardiovascular disease.

Keywords: Sodium glucose cotransporter 2 inhibitors, diabetes mellitus, empagliflozin, dapagliflozin, lipid panel

Öz

Amaç: Bu çalışmada, Tip-2 Diabetes Mellitus (T2DM) ile takipli ve empagliflozin veya dapagliflozin kullanan hastalarda 12 haftalık süreçte Sodyum Glukoz Kotransporter 2 inhibitörlerinin (SGLT-2i) günlük rutinde kullanılan bazı laboratuvar test sonuçları üzerindeki etkisini incelemeyi amaçladık .

Gereç ve Yöntem: T2DM (18 yaş üstü) ile takipli ve üçlü kombinasyon tedavisine SGLT-2i eklenen üç yüz on hasta bu çalışmaya dahil edildi. Mevcut tedavi rejimlerine ek olarak empagliflozin (günde bir kez 10 mg) (n : 170) veya dapagliflozin (günde bir kez 10 mg) (n: 140) alan hastalar iki gruba ayrıldı. Tüm hastaların laboratuvar bulguları tedavi öncesi ve 12 haftalık takip sonrasında kaydedildi .

Bulgular: Hem empagliflozin hem de dapagliflozin grupları , ortalama açlık kan şekeri ve HbA1c'de benzer iyileşme oranlarına sahipti. Empagliflozin grubuna kıyasla dapagliflozin grubunda lipid profillerinde ve spot idrar parametrelerinde yüksek düzeyde iyileşme saptandı . 12 haftalık takipte diğer laboratuvar parametrelerindeki değişiklik gruplar arasında anlamlı farklılık göstermedi. Toplam yan etkiler açısından tedavi grupları arasında fark gözlenmedi .

Sonuç: Empagliflozin ve dapagliflozin , 12 haftalık takipte açlık kan şekeri ve HbA1C üzerinde benzer etkilere sahipti. Özellikle kardiyovasküler hastalığı olan popülasyonda dapagliflozinin lipid profiline olan olumlu etkisi sebebiyle tercih sebebi olabileceği düşünülebilir.

Anahtar Kelimeler: Sodyum glukoz kotransporter 2 inhibitörleri , diabetes mellitus, empagliflozin , dapagliflozin , lipid paneli

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INTRODUCTION

Diabetes mellitus (DM) is a metabolic disease characterized by hyperglycemia and it occurs due to disturbances in the secretion of insulin or the effect of insulin on peripheral cells.[1] With the increasing prevalence of type 2 DM (T2DM), adequate glycemic control cannot be achieved in a significant percentage of patients, and the disease causes many comorbidities and life-threatening conditions, especially with the addition of renal and cardiac complications.[2,3] The change of lifestyle and oral anti-hyperglycemic drugs (OADs), which are generally used in first-line treatments, have prognostic importance in the management of T2DM. OADs, including Sodium Glucose Cotransporter 2 inhibitors (SGLT-2i), demonstrate anti-hyperglycemic effects with several different mechanisms.[4] SGLT-2i have high efficacy, safety, and tolerability profiles without significant risk of hypoglycemia and are generally considered as second or third-line anti-hyperglycemic drugs.[5] They can also be used in monotherapy when metformin is contraindicated.[6]

SGLT-2i (empagliflozin, dapagliflozin, etc.), which are frequently preferred in the treatment of T2DM, show cardio-protective and reno-protective effects.[7-9] This is associated with anti-hyperglycemic effects via the inhibition of sodium glucose reabsorption in the renal tubules independent of insulin. Thus, they are able to exert osmotic diuretic, natriuretic, and glycosuric effects.[10] Due to these effects, SGLT-2i increase sodium delivery to the macula densa and cause vasoconstriction in the afferent arteriole, contributing reno-protective effects by reducing the load on the glomeruli. They also show cardio-protective effects by reducing cardiac afterload.[11] Increasing evidence indicates that empagliflozin, which is a highly effective agent for secondary prevention, is a safer option in terms of both renoprotective and cardio-protective attributes.[12,13] However, there are limited studies evaluating the effects of empagliflozin and dapagliflozin on routine laboratory test results in the short term.

Therefore, in this study, we aimed to examine the effect of empagliflozin and dapagliflozin on some routine laboratory test results at 12 weeks of follow-up among T2DM patients using SGLT-2i.

MATERIAL AND METHOD

This study was planned as a single-center retrospective study between June 2019 and June 2020 in Ankara City Hospital. Sample size was calculated based on changes in HbA1c levels in the T2DM cohort at 12 weeks of follow-up in groups using empagliflozin and dapagliflozin. Accordingly, it was determined that at least 90 patients were required in both treatment groups to detect a difference of 0.4% with power of 90% and a significance level of 0.05 (assuming standard deviation of 1.2% and a correlation coefficient of 0.7). The study was approved by the Ankara City Hospital Ethics Committee (Date: 11.2021, Decision No: E2-21-99). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study population

Adults aged between 18 and 80 years with a diagnosis of T2DM who were treated with a stable triple combination therapy including the administration of metformin (2000 mg/day or maximum tolerated dose), glimepiride (8 mg/day or maximum tolerated dose), and dipeptidyl peptidase 4 inhibitors (100 mg/day sitagliptin/vildagliptin or maximum dose according to the local label) for 12 weeks before administration of an SGLT2i as well as lifestyle changes but who did not achieve glycemic control (hemoglobin A1c (HbA1c) of >7%) were evaluated. Three hundred ten T2DM patients using only triple oral antidiabetics with SGLT-2i added to their treatments were included in this study.

The following individuals were excluded from the study: female patients who were pregnant or lactating, and those who had experienced gestational diabetes; patients with type 1 diabetes; patients with a history of cancer or currently undergoing anticancer treatment; those with chronic pancreatitis, steroid-induced diabetes mellitus, Cushing's syndrome, acromegaly, abnormal serum creatinine levels (>1.5 mg/dL in men and >1.4 mg/dL in women), serum aspartate transaminase (AST) or alanine transaminase (ALT) levels 3 times the upper limit of the normal range, previous history of SGLT2i treatment, glomerular filtration rate of <45, history of diabetic ketoacidosis, genitourinary system infection, or acute renal failure; and individuals using, angiotensin converting enzyme inhibitor (ACEI), angiotensinogen receptor blocker (ARB) and diuretic drugs.

Study Protocol

Clinical, demographic, and laboratory findings were recorded from the hospital's automation system and patient files. Patients who received either empagliflozin (10 mg once daily) or dapagliflozin (10 mg once daily) in addition to their current treatment regimen were divided into two groups. Laboratory findings of all patients were recorded before treatment and at the end of 12 weeks of follow-up.

Laboratory parameters

In the morning, fasting blood samples were drawn for biochemical parameters and other laboratory parameters. After the blood samples were centrifuged at 2500×g for 10 minutes, plasma and serum samples were separated. All parameters were evaluated from the same laboratory. Serum glucose, serum electrolytes, ALT, AST, GGT, ALP was measured on a Beckman Coulter AU 5800 autoanalyzer (Beckman Coulter Inc., Brea, CA, USA) using the enzymatic ultraviolet hexokinase method. HbA1c was measured by cation-exchange high-performance liquid chromatography method using the ARKRAY ADAMS A1c HA8180 automated glycohemoglobin analyzer (ARKRAY Global Business

Inc., Kyoto, Japan). Urine albumin levels were evaluated with Novatrend TM Fluorescence Immunoassay Analyzer. Albumin was measured using the bromocresol green method. Total cholesterol was measured by enzymatic colorimetric method and high-density lipoprotein cholesterol (HDL-C) was measured by enzymatic colorimetric method with a Hitachi modular autoanalyzer (Roche Diagnostic Corp., Indianapolis, IN, USA). Low-density lipoprotein cholesterol (LDL-C) level was calculated with the Friedewald formula for patients with triglyceride concentrations of <400 mg/dL.[14] Patients with triglyceride concentrations of >400 mg/dL were evaluated by enzymatic colorimetric method with the second-generation LDL-C Plus Kit and the Hitachi Modular P800 (Roche Diagnostic Corp., Indianapolis, IN, USA).

Endpoints and assessments

The primary and secondary endpoints in this study were calculated by subtracting 12-week values from baseline values for the empagliflozin and dapagliflozin groups. The primary endpoint was assessed as changes in HbA1c, fasting plasma glucose (FPG) levels, lipid profiles and other laboratory parameters. Secondary endpoints were evaluated adverse events like dysuria, dyspepsia, urinary tract infection.

Statistical analysis

The STATA program (StataCorp LLC, College Station, TX, USA) was used for data analysis. Normality testing was performed with the Shapiro–Wilk test. Normal distributions were shown as mean±standard deviation and non-normal distributions as median (interquartile range: 25^{th}-75^{th} percentile). Categorical variables were expressed as numbers and percentages. Student's T test or the Mann–Whitney U test was used to compare numerical variables between the AR and RR groups. Chi-square, Yates correction, and Fisher's exact chi-square tests were used for comparisons of categorical data. Changes of laboratory parameters at the 12 weeks compared to baseline were evaluated by repeated measures for ANOVA analysis. The effect of potential risk factors contributing to the change in CMR parameters were examined by multivariate linear regression analysis. Values of p<0.05 (*) were considered significant in statistical analysis.

RESULTS

The mean age of study population was 51.9±8.7 years and consisted mostly of males (65.8%) with a representative risk profile for T2DM. SGLT-2i distributions were 54.8% (n:170) empagliflozin and 45.2% (n:140) dapagliflozin. Demographic characteristics were no significant difference in empagliflozin and dapagliflozin groups (**Table 1**).

Table 1. Demographic characteristics of patients with Type 2 diabetes mellitus

Variables	All population n=310	Empagliflozin n=170	Dapagliflozin n=140	P
Age, years	51.9±8.7	50.9±9.7	52.8±7.8	0.278
Gender, n(%)				
Male	204 (65.8)	111 (65.3)	93 (66.4)	0.834
Female	106 (34.2)	59 (34.7)	47 (33.6)	
BMI, kg/m2	28.6±3.0	28.9±3.6	28.3±2.5	0.299
Smoking, n(%)	83 (26.8)	42 (24.7)	41 (29.3))	0.365
Alcohol use, n(%)	16 (5.2)	8 (4.7)	8 (5.7)	0.798
Comorbidity, n(%)				
CHD	31 (10.0)	20 (11.8)	11 (7.9)	0.342
Lung disease	23 (7.4)	12 (7.1)	11 (7.9)	0.830
Thyroid disease	30 (9.7)	14 (8.2)	16 (11.4)	0.441
Hyperlipidemia	167 (53.9)	89 (52.4)	78 (55.7)	0.555
Anemia	18 (5.8)	9 (5.3)	9 (6.4)	0.808
Drugs, n(%)				
Metformin	292 (94.2)	159 (93.5)	133 (95.0)	0.633
Sulfonylurea	49 (15.8)	23 (13.5)	26 (18.6)	0.274
DPI	74 (23.9)	43 (25.3)	31 (22.1)	0.517
Glitazone	4 (1.3)	4 (2.4)	-	0.186
Glinide	4 (1.3)	-	4 (2.9)	0.087
Insulin	49 (15.8)	25 (14.7)	24 (17.1)	0.639
Non-steroid	36 (11.6)	16 (9.4)	20 (14.3)	0.214
PPIs	75 (24.2)	45 (26.5)	30 (21.4)	0.302
Statin	86 (27.7)	45 (26.5)	41 (29.3)	0.582

Data are mean±standard deviation, median (IQR), or number (%). *, considered statistically significant (p<0.05). Abbreviations: CHD, coronary heart disease; DPI, dry powder inhaler; PPI, proton pump inhibitors

Mean total cholesterol (191.3±27.3 vs 214.0±39.6; P=0.001), median LDL–C (106.3±22.9 vs 130.0±30.3; P<0.001), median triglyceride (153.5 vs 204.5; P=0.029), median urine protein (69 vs 161; P<0.001), median microalbumin (10.8 vs 27.7; P=0.033) baseline levels were lower in empagliflozin group compared to dapagliflozin group. Other laboratory findings were no significant difference in empagliflozin and dapagliflozin groups (**Table 2**).

At 12 weeks follow-up, changes in short-term laboratory findings in patients with SGLT-2i treatment are shown in detail in **Table 2**. In both SGLT-2i treatment groups, mean hemoglobin levels, mean UREA levels, mean phosphorus levels, and mean calcium levels were higher on 12 weeks compared to baseline, and FPG, HbA1C, gamma glutamyl transferase, and urine microalbumin to creatinine ratios were lower (P<0.05) and these changes were similar between the two groups (ΔP>0.05).

In dapagliflozin groups, mean total cholesterol levels (214.0±39.6 vs 190.0±34.4; P<0.001), median LDL (130.0±30.3 vs 98.1±20.7; P=0.002), median triglyceride levels (204.5 vs 154; P<0.001), median urine protein levels (161 vs 110.7; P<0.001), and median urine protein to creatinine ratio levels (108 vs 80; p=0.048) were lower on 12 weeks compared to baseline, while mean HDL – C levels was higher (45.8±9.5 vs 48.7±8.0; P=0.013). These parameters did not change in empagliflozin group (**Table 2**).

Table 2. Changes in short-term laboratory findings in patients added to SGLT-2i treatment

Variables	Empagliflozin n=170			Dapagliflozin n=140			P1	P2
	Baseline	12 weeks	P	Baseline	12 weeks	P		
Hemoglobin, g/dL	14.4±1.2	14.9±1.3	<0.001*	14.6±1.4	15.2±1.4	<0.001*	0.303	0.601
WBC, x10^3 /mL	7.8±2.2	7.7±1.6	0.826	7.9±1.9	7.8±1.6	0.662	0.819	0.931
Neutrophil, x10^3 /mL	4 (3.3-5.4)	4.2 (3.4-5.2)	0.273	4.2 (3.4-5.2)	4.1 (3.4-5.3)	0.907	0.731	0.339
Lymphocyte, x10^3 /mL	2.6±0.7	2.4±0.6	0.067	2.7±0.6	2.7±0.8	0.824	0.451	0.120
Platelet, x10^3 /mL	276.5±62.1	271.6±65.0	0.299	267.8±68.7	270.6±73.1	0.540	0.515	0.241
FPG, mg/dL	160.5 (125-204)	129.5 (102-151)	<0.001*	172 (135-209)	133 (116-156)	<0.001*	0.326	0.747
HbA1c, %	9.1±1.9	7.6±1.1	<0.001*	9.3±1.4	7.6±0.7	<0.001*	0.388	0.355
Urea, mg/dL	32.0±9.2	35.6±7.1	0.044*	31.2±7.3	35.5±9.0	<0.001*	0.341	0.395
Creatinine, mg/dL	0.8±0.1	0.8±0.2	0.611	0.8±0.1	0.8±0.1	0.690	0.705	0.126
eGFR, mL/dk/1.73 m²	99.3±10.0	97.6±13.6	0.241	97.1±10	96.5±13.5	0.811	0.289	0.350
Sodium, mmol/L	139.2±2.5	139.4±1.7	0.690	139.7±2.5	139.7±1.8	0.953	0.407	0.850
Potassium, mmol/L	4.5±0.4	4.4±0.3	0.089	4.5±0.4	4.4±0.4	0.121	0.841	0.870
Phosphorus, mg/dL	3.7±0.5	4.0±0.7	0.010*	3.5±0.5	3.8±0.5	<0.001*	0.165	0.533
Magnesium, mg/dL	1.8±0.4	1.9±0.2	0.134	1.9±0.2	1.9±0.2	0.146	0.418	0.729
Calcium, mg/dL	9.6±0.4	9.8±0.5	0.033*	9.6±0.4	9.8±0.5	0.005*	0.286	0.709
Total protein, mg/dL	7.1±0.3	7.1±0.5	0.845	7.0±0.5	7.1±0.4	0.103	0.373	0.716
Uric acid, mg/dL	4.7 (3.7-5.7)	4.7 (3.7-5.1)	0.863	4.4 (3.8-5.0)	4.3 (3.8-5.6)	0.891	0.117	0.747
Albumin, g/dL	4.7±0.3	4.7±0.3	0.103	4.7±0.3	4.7±0.3	0.101	0.150	0.875
Total cholesterol, mg/dL	191.3±27.3	186.4±41.8	0.344	214.0±39.6	190.0±34.4	<0.001*	0.001*	0.040*
HDL, mg/dL	44.8±9.8	45.8±10.5	0.198	45.8±9.5	48.7±8.0	0.013*	0.615	0.046*
LDL, mg/dL	106.3±22.9	103.4±32.0	0.469	130.0±30.3	98.1±20.7	<0.001*	<0.001*	<0.001*
Triglyceride, mg/dL	153.5 (117-270.5)	152 (97-197)	0.145	204.5 (137-321)	154 (119-185)	<0.001*	0.029*	0.023*
ALT, U/L	30 (20-44)	28 (21-36)	0.507	27 (20-42)	25 (21-35)	0.118	0.843	0.264
AST, U/L	21 (16-30)	18 (13-24)	0.105	20 (15-25)	17 (13-22)	0.101	0.311	0.636
GGT, U/L	34 (21-48)	28.5 (20-47)	0.046*	36 (24-58)	28 (19-49)	0.001*	0.543	0.691
ALP, U/L	84 (72-102)	80 (68-89)	0.122	84 (66-105)	79 (62-89)	0.105	0.878	0.775
Urine protein, mg/L	69 (58.3-112.8)	80.2 (59.1-111.3)	0.768	161 (80.3-200.1)	110.7 (79.6-143)	0.002*	<0.001*	0.042*
Urine creatinine, mg/dL	82.9 (36.2-141.2)	83.6 (64.4-103.1)	0.739	93.7 (37.8-178)	92.0 (78.2-118)	0.271	0.236	0.747
Urine mA, mg/L	10.8 (5-29.7)	7.3 (3.4-14.2)	0.011*	27.7 (9.6-38.6)	4.7 (2.9-15)	<0.001*	0.033*	0.028*
Urine PCR, mg/g cr	98 (69-123)	97.5 (68-129)	0.655	108 (79-132)	80 (66-112)	0.048*	0.212	0.035*
Urine mACR, mg/g cr	14.1 (4.4-27.7)	7.6 (3.9-12.8)	0.025*	10.2 (6.8-20.5)	4.8 (3-9.9)	0.038*	0.779	0.292

Data are mean±standard deviation, median (IQR), or number (%). *, considered statistically significant (p<0.05). P1, baseline laboratory findings in Empagliflozin vs Dapagliflozin; P2, change of laboratory findings in Empagliflozin vs Dapagliflozin. Abbreviations: WBC, white blood count, FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; eGFR, estimated glomerular filtration rate; HDL, high density lipoprotein; LDL, low density lipoprotein; ALT, alanin aminotransferaz; AST, aspartate aminotransferase; GGT; gamma glutamyl transferase, ALP, alkalen fosfataz

The incidence of adverse events was 31.7% (n:97), and the most common were dysuria (15.2%), dyspepsia (11.3%), and urinary tract infection (7.1%). Adverse event and its subtypes did not differ significantly in the SGLT-2i treatment groups (**Table 3**).

Table 3. Advers Events

Adverse Effects	All population n=310	Empagliflozin n=170	Dapagliflozin n=140	P
Dysuria, n(%)	47(15.2)	26(15.3)	21(15.0)	0.999
Dyspepsia, n(%)	35(11.3)	20(11.8)	15(10.7)	0.858
Urinary tract infection, n(%)	22(7.1)	13(7.6)	9(6.4)	0.825
Vaginitis, n(%)	3(1.0)	1(0.6)	2(1.4)	0.866
Back/Hip pain, n(%)	3(1.0)	0	3(2.1)	0.182
Documented hypoglycemia, n(%)	2(0.6)	0	2(1.4)	0.395
Weight gain, n(%)	2(0.3)	2(1.2)	0	0.503
Total adverse effects, n(%)	97(31.7)	54(31.8)	43(30.7)	0.843

Data are number (%).

DISCUSSION

In this study, the short-term effects of empagliflozin and dapagliflozin as adjunctive therapy for patients with lifestyle changes and T2DM who experienced inadequate glycemic control with traditional first-line OADs were evaluated. Both empagliflozin and dapagliflozin had similar profiles of improvement of mean FPG, and HbA1c. However, dapagliflozin was associated with a more significant improvement in lipid profiles and spot urinary parameters compared to empagliflozin. In terms of total side effects, no difference was observed between treatment groups.

The progressive nature of diabetes necessitates changes in treatment regimens over time and combination therapy is needed due to the fact that it is usually difficult to achieve the desired glycemic control with monotherapy.[15] It has been reported in previous clinical studies that SGLT-2i are effective in controlling blood glucose levels, reducing body weight, and achieving glycemic control without serious side effects.[16-19] Failure to achieve glycemic control in cases

of T2DM, particularly in terms of high HbA1c levels, may cause an increased risk of cardiovascular and renal disease complications.[20,21] Therefore, HbA1c levels are of prognostic importance in T2DM.[22]

Our results show that empagliflozin and dapagliflozin have similar efficacy in significantly reducing HbA1c in the short term. This efficacy differs from the findings of previous studies. In the studies conducted by Ku et al.[12] and Hussain et al.[13] it was reported that empagliflozin reduced body weight, blood glucose levels, and HbA1c more than dapagliflozin while improving cardio-metabolic risk factors more and reducing the incidence of genitourinary infections. The difference in our study suggests that the two treatment groups with similar mechanisms may have similar efficacy in the short term. Urinary tract infections are a common side effect of SGLT-2i treatment. The difference in our study suggests that the two treatment groups with similar mechanisms may have similar efficacy in the short term. The basis of the proposed pathophysiological mechanism is that glycosuria caused by SGLT2i provides a positive environment for bacterial growth in the urinary tract.[23] In a meta-analysis, only the relationship between dapagliflozin, among all considered SGLT2i, and urinary tract infections was dose-dependent.[24] The dapagliflozin group in our study may explain the low observed frequency of urinary tract infections. However, we think that dyspepsia, which is the most common secondary side effect, is more generally related to metformin.[25,26]

Impaired lipid metabolism in T2DM patients is associated with an increased risk of cardiovascular disease, including atherosclerosis.[27] SGLT2i may affect lipid metabolism, which plays an important role in linking insulin resistance to cardiac injury and even in the development of cardiovascular diseases.[28] In a study conducted with T2DM patients using DPP-4 inhibitors and dapagliflozin, it was reported that dapagliflozin was associated with a significant increase in HDL-C levels.[29] In an experimental study, it was determined that empagliflozin was associated with an increase in LDL-C levels.[30] This effect of empagliflozin was explained by the induction of the transition from carbohydrate to lipid usage for energy in the fasting state.[31] Our findings have shown that patients who received dapagliflozin had worse lipid profiles at baseline but greater improvement in lipid profiles at the 12-week follow-up, whereas those who received empagliflozin did not show a difference in improvement. A possible explanation for this might be differences in pharmacokinetic properties and SGLT2/SGLT1 receptor selectivity. Sodium excretion and osmotic diuresis effects of dapagliflozin are longer-lasting.[31] However, the SGLT2:SGLT1 receptor selectivity ratio of dapagliflozin is approximately half that of empagliflozin.[32] SGLT1 receptors are mostly located in the bowel, and higher selectivity may reduce postprandial blood sugar variations, which may play a helpful role in lowering the risk of heart failure.[33]

SGLT-2i reduce cardiovascular events and may delay the progression of renal disease in patients with T2DM and cardiovascular comorbidities.[34,35] SGLT-2i significantly reduces albuminuria, decreasing the extent of its toxic effects on the renal tubules. This is largely due to the reduction in intraglomerular pressure.[36] Although higher urinary microalbuminuria was initially observed in those receiving dapagliflozin, a greater reduction was found in follow-up. It is thought that this decrease in urinary microalbuminuria was due to a decrease in high levels of advanced glycation end productsdue to blood sugar regulation, decreased oxidative stress, and decreased blood pressure in the afferent arterioles in the proximal renal tubules. This is consistent with the mechanism of dapagliflozin described above. In addition, an increase in Hgb was observed with a possible increase in erythropoietin in patients using SGLT-2i.[37] In our study, there was a moderate increase in serum phosphate and calcium levels, probably due to increased renal tubular phosphate reabsorption.[38] As a result of the weight loss effects of SGLT-2i., a decrease in ggt levels was detected. It can also be said that ggt, which increases in case of inflammation, regresses due to the anti-inflammatory effect of sglt2.[39]

The important limitations of this study are that it was retrospective and was conducted with a limited number of patients. Another limitation of ours is that the effect of SGLT-2i on laboratory findings was examined in a short period of 12 weeks.

CONCLUSIONS

According to the results of our study, we can say that both SGLT-2i have positive effects on blood sugar and lipid panel, while they have neutral effects on other laboratory parameters. However, a much larger sample and a much longer observation period are required to examine such results more effectively.

List of Abbreviations

ACEI: Angiotensin converting enzyme inhibitor, **ALT:** Alanine transaminase, **ARB:** Angiotensinogen receptor blocker, **AST:** Aspartate transaminase, **DM:** Diabetes mellitus , **FPG:** Fasting plasma glucose, **HbA1c:** Hemoglobin A1c, **HDL-C:** High-density lipoprotein cholesterol, **LDL-C:** Low-density lipoprotein cholesterol, **OADs:** Oral anti-hyperglycemic drugs, **SGLT-2i:** Sodium glucose cotransporter 2 inhibitor, **T2DM:** Type 2 diabetes mellitus

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by the Ankara City Hospital Ethics Committee (Date: 11.2021, Decision No: E2-21-99).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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