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

SGLT-2 İhibitörleri’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 sürede Sodyum Glukoz Kotransporter 2 inhibitörlerinin (SGLT-2) 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 çalışmayı 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.


Sonuç: Empagliflozin ve dapagliflozin, 12 haftalık takipte açlıkkan şeker ve HbA1c’dede benzer iyileşme oranlarını sahipti. Özellikle kardiyovasküler hastalığı olan populasyonda dapagliflozinin lipid profiline olan olumlu etkisi sebebiyle tercih sebebi olabileceğini düşünebilir.

Anahtar Kelimeler: Sodyum glukoz kotransporter 2 inhibitörleri, diabetes mellitus, empagliflozin, dapagliflozin, lipid paneli
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 renoprotective 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 renoprotective 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 H8180 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. 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: 25th–75th 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>
<thead>
<tr>
<th>Variables</th>
<th>All population</th>
<th>Empagliflozin n=310</th>
<th>Dapagliflozin n=140</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>51.9±8.7</td>
<td>50.9±9.7</td>
<td>52.8±7.8</td>
<td>0.278</td>
</tr>
<tr>
<td>Gender, n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>204 (65.8)</td>
<td>111 (65.3)</td>
<td>93 (66.4)</td>
<td>0.834</td>
</tr>
<tr>
<td>Female</td>
<td>106 (34.2)</td>
<td>59 (34.7)</td>
<td>47 (33.6)</td>
<td></td>
</tr>
<tr>
<td>BMI, kg/m2</td>
<td>28.6±3.0</td>
<td>28.4±3.6</td>
<td>28.3±2.5</td>
<td>0.299</td>
</tr>
<tr>
<td>Smoking, n(%)</td>
<td>83 (26.8)</td>
<td>42 (24.7)</td>
<td>41 (29.3)</td>
<td>0.365</td>
</tr>
<tr>
<td>Alcohol use, n(%)</td>
<td>16 (5.2)</td>
<td>8 (4.7)</td>
<td>8 (5.7)</td>
<td>0.798</td>
</tr>
<tr>
<td>Comorbidities, n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHD</td>
<td>31 (10.0)</td>
<td>20 (11.8)</td>
<td>11 (7.9)</td>
<td>0.342</td>
</tr>
<tr>
<td>Lung disease</td>
<td>23 (7.4)</td>
<td>12 (7.1)</td>
<td>11 (7.9)</td>
<td>0.830</td>
</tr>
<tr>
<td>Thyroid disease</td>
<td>30 (9.7)</td>
<td>14 (8.2)</td>
<td>16 (11.4)</td>
<td>0.441</td>
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<tr>
<td>Hyperlipidemia</td>
<td>167 (53.9)</td>
<td>89 (52.4)</td>
<td>78 (55.7)</td>
<td>0.555</td>
</tr>
<tr>
<td>Anemia</td>
<td>18 (5.8)</td>
<td>9 (5.3)</td>
<td>9 (6.4)</td>
<td>0.808</td>
</tr>
<tr>
<td>Drugs, n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metformin</td>
<td>292 (94.2)</td>
<td>159 (93.5)</td>
<td>133 (95.0)</td>
<td>0.633</td>
</tr>
<tr>
<td>Sulfonylurea</td>
<td>49 (15.8)</td>
<td>23 (13.5)</td>
<td>26 (18.6)</td>
<td>0.274</td>
</tr>
<tr>
<td>DPI</td>
<td>74 (23.9)</td>
<td>43 (25.3)</td>
<td>31 (22.1)</td>
<td>0.517</td>
</tr>
<tr>
<td>Glitazone</td>
<td>4 (1.3)</td>
<td>4 (2.4)</td>
<td>-</td>
<td>0.186</td>
</tr>
<tr>
<td>Glinide</td>
<td>4 (1.3)</td>
<td>-</td>
<td>4 (2.9)</td>
<td>0.087</td>
</tr>
<tr>
<td>Insulin</td>
<td>49 (15.8)</td>
<td>25 (14.7)</td>
<td>24 (17.1)</td>
<td>0.639</td>
</tr>
<tr>
<td>Non-steroid</td>
<td>36 (11.6)</td>
<td>16 (9.4)</td>
<td>20 (14.3)</td>
<td>0.214</td>
</tr>
<tr>
<td>PPIs</td>
<td>75 (24.2)</td>
<td>45 (26.5)</td>
<td>30 (21.4)</td>
<td>0.302</td>
</tr>
<tr>
<td>Statin</td>
<td>86 (27.7)</td>
<td>45 (26.5)</td>
<td>41 (29.3)</td>
<td>0.582</td>
</tr>
</tbody>
</table>

Data are mean±standard deviation, median (QR), 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).
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. Adverse Events

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

### DISCUSSION

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. 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. Failure to achieve glycemic control in cases

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

<table>
<thead>
<tr>
<th>Variables</th>
<th>Empagliflozin n=170</th>
<th>Dapagliflozin n=140</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin, g/dL</td>
<td>14.4±1.2</td>
<td>14.9±1.3</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>WBC, x10³/mL</td>
<td>7.8 ±2.2</td>
<td>7.7 ±1.6</td>
<td>0.826</td>
</tr>
<tr>
<td>Neutrophil, x10³/mL</td>
<td>4.3 (3.5-5.4)</td>
<td>4.2 (3.5-5.2)</td>
<td>0.273</td>
</tr>
<tr>
<td>Lymphocyte, x10³/mL</td>
<td>2.6 ±0.7</td>
<td>2.4 ±0.6</td>
<td>0.067</td>
</tr>
<tr>
<td>Platelet, x10³/mL</td>
<td>276±62 ±1</td>
<td>271±65 ±0</td>
<td>0.299</td>
</tr>
<tr>
<td>FPG, mg/dL</td>
<td>160.5 (125-204)</td>
<td>129.5 (102-151)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>9.1±1.9</td>
<td>7.6±1.1</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Urea, mg/dL</td>
<td>32.0±9.2</td>
<td>35.6±7.1</td>
<td>0.044*</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>0.8±0.1</td>
<td>0.8±0.2</td>
<td>0.611</td>
</tr>
<tr>
<td>eGFR, mL/dL/1.73 m²</td>
<td>99.3±10.0</td>
<td>97.6±13.6</td>
<td>0.241</td>
</tr>
<tr>
<td>Sodium, mmol/L</td>
<td>139.2±2.5</td>
<td>139.4±1.7</td>
<td>0.690</td>
</tr>
<tr>
<td>Potassium, mmol/L</td>
<td>4.5±0.4</td>
<td>4.4±0.3</td>
<td>0.089</td>
</tr>
<tr>
<td>Phosphorous, mg/dL</td>
<td>3.7±0.2</td>
<td>4.0±0.7</td>
<td>0.010*</td>
</tr>
<tr>
<td>Magnesium, mg/dL</td>
<td>1.8±0.4</td>
<td>1.9±0.2</td>
<td>1.000</td>
</tr>
<tr>
<td>Calcium, mg/dL</td>
<td>9.6±0.6</td>
<td>9.8±0.5</td>
<td>0.351</td>
</tr>
<tr>
<td>Total protein, mg/dL</td>
<td>7.1±0.3</td>
<td>7.1±0.5</td>
<td>0.845</td>
</tr>
<tr>
<td>Uric acid, mg/dL</td>
<td>4.7 (3.7-5.7)</td>
<td>4.7 (3.7-5.1)</td>
<td>0.863</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>4.7±0.3</td>
<td>4.7±0.3</td>
<td>0.103</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>191.3±27.3</td>
<td>186.4±41.8</td>
<td>0.344</td>
</tr>
<tr>
<td>HDL, mg/dL</td>
<td>44.8±9.8</td>
<td>45.8±10.5</td>
<td>0.198</td>
</tr>
<tr>
<td>LDL, mg/dL</td>
<td>106.3±22.9</td>
<td>103.4±32.0</td>
<td>0.469</td>
</tr>
<tr>
<td>Triglyceride, mg/dL</td>
<td>153.5 (117-270.5)</td>
<td>152 (97-197)</td>
<td>0.145</td>
</tr>
<tr>
<td>ALT, U/L</td>
<td>30 (20-44)</td>
<td>28 (21-36)</td>
<td>0.507</td>
</tr>
<tr>
<td>AST, U/L</td>
<td>21 (16-30)</td>
<td>18 (13-24)</td>
<td>0.105</td>
</tr>
<tr>
<td>GGT, U/L</td>
<td>34 (21-48)</td>
<td>28.5 (20-47)</td>
<td>0.046*</td>
</tr>
<tr>
<td>ALP, U/L</td>
<td>84 (72-102)</td>
<td>80 (68-89)</td>
<td>0.122</td>
</tr>
<tr>
<td>Urine protein, mg/L</td>
<td>69 (58.3-112.8)</td>
<td>80.2 (59.1-111.3)</td>
<td>0.768</td>
</tr>
<tr>
<td>Urine creatinine, mg/dL</td>
<td>82.9 (36.2-141.2)</td>
<td>83.6 (64.4-103.1)</td>
<td>0.739</td>
</tr>
<tr>
<td>Urine mA, mg/L</td>
<td>10.8 (5-29.7)</td>
<td>7.3 (3.4-14.2)</td>
<td>0.011*</td>
</tr>
<tr>
<td>Urine PCR, mg/g cr</td>
<td>98 (69-123)</td>
<td>97.5 (68-129)</td>
<td>0.655</td>
</tr>
<tr>
<td>Urine uAMCR, mg/g cr</td>
<td>14.1 (4.4-27.7)</td>
<td>7.6 (3.9-12.8)</td>
<td>0.025*</td>
</tr>
</tbody>
</table>

Data are mean ±standard deviation, median (IQR), or number (%). * considered statistically significant (p<0.05). P: 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, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma glutamyl transferase; ALP, alkaline fosfatase.
of T2DM, particularly in terms of high HbA1c levels, may cause an increased risk of cardiovascular and renal disease complications. Therefore, HbA1c levels are of prognostic importance in T2DM.

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. and Hussain et al., 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. In a meta-analysis, only the relationship between dapagliflozin, among all considered SGLT2i, and urinary tract infections was dose-dependent. 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.

Impaired lipid metabolism in T2DM patients is associated with an increased risk of cardiovascular disease, including atherosclerosis. 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. 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. In an experimental study, it was determined that empagliflozin was associated with an increase in LDL-C levels. This effect of empagliflozin was explained by the induction of the transition from carbohydrate to lipid usage for energy in the fasting state. 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. However, the SGLT2/SGLT1 receptor selectivity ratio of dapagliflozin is approximately half that of empagliflozin. 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.

SGLT-2i reduce cardiovascular events and may delay the progression of renal disease in patients with T2DM and cardiovascular comorbidities. 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. 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 products due 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. In our study, there was a moderate increase in serum phosphate and calcium levels, probably due to increased renal tubular phosphate reabsorption. 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.

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


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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