



Review

Lipid profile in type 2 diabetic patients with new dapagliflozin treatment; actual clinical experience data of six months retrospective lipid profile from single center

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ABSTRACT

Introduction: Dapagliflozin is a sodium–glucose cotransporter 2 inhibitor that improves glycemic control in patients with type II diabetes mellitus which increasing urinary glucose excretion. With numerous controlled experimental studies of dapagliflozin, evaluation of real-life data after entry into clinical practice is an important condition. In our study, the effects of dapagliflozin (10 mg) on lipid profile were investigated retrospectively.

Methods: A total of thirty-one type 2 diabetic patients with HbA1c level between 6,5% and 13%, aged 45–80 years and whose body mass index higher than 20 kg/m² were enrolled to the study. Data before dapagliflozin treatment and three and six months results were recorded.

Results: Dapagliflozin reduced HbA1c levels by 0,9% at 3 months and 0,79% at 6 months. Total cholesterol level decreased 17,6 mg/dl, LDL cholesterol level decreased 13,4 mg/dl and triglyceride level by 25.9 mg/dl at the 6th months and it is observed that there is no serious side effect on the usage for 6 months.

Conclusion: There are conflicting results about the effect of SGLT2 inhibitors on the lipid profile in the literature. According to our data, dapagliflozin has positive effects on lipid profile as weight and glycemic control and it is well tolerated. Therefore, dapagliflozin therapy is beneficial because of the positive change in lipid profile and weight loss in diabetic patients with overweight and hyperlipidemia.

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1. Introduction

Diabetes is a chronic metabolic disorder that requires continuous medical care, where the organism cannot adequately use carbohydrate, fats and proteins due to insufficient insulin or defect in insulin [1]. Diabetes is one of the most significant global health emergencies of the 21st century. In 2014, 9.3% of the entire population in the United States of America was diagnosed with diabetes and the diabetic population reached 29.81 million [3]. According to the International Diabetes Federation (IDF), some 425 million people worldwide, or 8.8% of adults 20–79 years, are estimated to have diabetes which total is set to reach 629 million by 2045 [2]. When not appropriately managed, all types of diabetes can result in complications affecting many parts of the body, leading to frequent hospitalization and early death [2]. In 2017, about 4 million people

died due to diabetes [2]. Despite all the precautions in the last 12 years, the prevalence of DM in our country is about two times higher. Despite all treatments, glycemic control is still not achieved in approximately % 72 of diabetic patients and many different treatment options continue to be developed.

Sodium-glucose cotransporter-2 (SGLT-2) is responsible for 90% of glucose reabsorption in proximal tubules [4,5]. Blocking SGLT-2 via selective inhibitors, SGLT-2 inhibitors increase glucose excretion from the body, reducing hyperglycemia. To increase urinary glucose excretion, SGLT-2 inhibitors lower glycemia without inducing excessive insulin secretion [6]. Dapagliflozin is the first SGLT-2 inhibitor drug approved in the European Union in 2012 and the United States in 2014 for use in diabetes [7]. SGLT-2 inhibitors offer a new treatment option independent of insulin action. SGLT-2 inhibitors are especially beneficial in the treatment of overweight or obese diabetic patients due to beneficial effects on weight [8]. While positive effects on weight have been determined more steadily, the effects on lipid are not consistent in studies.

In this study, changes in lipid profile were evaluated

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retrospectively in patients using dapagliflozin from single centered real-life data. When the literature is reviewed, it is seen that there are few studies on the use of dapagliflozin with real-life data. This study aimed to give an idea about the effects of dapagliflozin (10 mg) on lipid profile in the treatment of diabetes and to contribute to the literature.

2. Methods

A total of 31 patients, 22 female and 9 male, were included in the study. The data files of the patients were obtained through detailed examination. The presence of hypertension, the duration of diabetes and the medications used were recorded and detailed. Anthropometric data of patients which measured and recorded at examination and data of the fasting plasma glucose, postprandial plasma glucose and HbA1c values measured at our center were recorded and used as glycemic control parameters. Total cholesterol, LDL (Low-Density Lipoprotein) cholesterol and triglyceride levels in lipid profile were evaluated. Pre-dapagliflozin, third and sixth months of treatment data of patients were included in the evaluation.

3. Statistical analysis

All data were transferred to the computer and analyzed for statistical analysis using the application-statistical analysis program of SPSS for Windows, version 23 (IBM Corporation, New York, United States), which accessible from our network. Independent sample T-test or Mann Whitney U variance analysis test was used for according to the provision of the normal distribution assumption. To compare numerical data in dependent groups, dependent sample T-test or Wilcoxon test was used according to the provision of the normal distribution assumption. As the descriptive values, the mean (+/- standard deviation) or median (min-max) according to the distribution of the data for the continuous variables (such as fasting plasma glucose, postprandial plasma glucose, weight), and the number (n) and percentage (%) values for the categorical variables (sex, etc.) were given. The significance level of p-value less than 0.05 was regarded as statistically significant.

4. Results

The number of patients under 55 years old was 15 (48%) and the number of patients over 55 years old was 16 (52%). Seventeen of the patients had a history of hypertension while fourteen of the patients had no history of hypertension. The number of patients with disease duration less than ten years was 14 (45%), while the number of patients with disease duration of 10 years and over was 17 (55%). A total of eight patients were on the treatment of insulin and oral antidiabetic (OAD), while 23 patients were on OAD combination without insulin.

Table 1 shows the baseline characteristics and averages of the parameters investigated in the patients who started dapagliflozin, and the distributions of these values regarding both men and women are also shown in the same table. In Table 2 and Table 3, three and six-month mean differences were given together with the measured third and sixth-month values after the using dapagliflozin.

Total cholesterol, LDL cholesterol and triglyceride were assessed in the lipid profile and the mean values before the onset of the drug were 217.3 mg/dL (± 43.4), 134.1 mg/dL (± 41.2) and 188.4 mg/dL (± 82.6) respectively.

There was a mean reduction 3.3 kg (± 2.5) in weight, 1.3 m (± 1.3) in waist circumference and 1.3 kg/m² (± 1) in BMI at the 3rd month. These changes were statistically significant ($p < 0.001$). There was

Table 1

Baseline characteristics of the full analysis.

	All patients	Men	Women
Age (years)	57,39 ($\pm 9,2$)	60,2 (± 10)	56,2 ($\pm 8,9$)
Weight (kg)	87,4 ($\pm 17,8$)	93,1 ($\pm 15,6$)	85 ($\pm 18,4$)
BMI (kg/m ²)	33,2 ($\pm 6,8$)	32 ($\pm 5,4$)	33,7 ($\pm 7,3$)
Waist circumference (cm)	106,4 ($\pm 15,3$)	108,1 ($\pm 10,6$)	105,7 (± 17)
HbA1c (%)	8,5 ($\pm 1,9$)	8,2 (± 2)	8,6 ($\pm 1,9$)
FPG (mg/dl)	192,7 ($\pm 62,6$)	180 ($\pm 43,6$)	198 ($\pm 69,1$)
PPG (mg/dl)	269 ($\pm 79,2$)	238,1 ($\pm 50,9$)	281,7 (± 86)
T. cholesterol (mg/dl)	217,3 ($\pm 43,4$)	208 (± 46)	221,1 ($\pm 42,9$)
LDLc (mg/dl)	134,1 ($\pm 41,2$)	127,8 ($\pm 43,1$)	136,7 ($\pm 41,1$)
Triglyceride (mg/dl)	188,4 ($\pm 82,6$)	173,5 ($\pm 64,9$)	194,5 ($\pm 89,5$)

BMI:Body mass indeks, FPG:Fasting plasma glucose, PPG:postprandial plasma glucose T. cholesterol: total cholesterol, LDLc: Low Density Lipoprotein cholesterol.

an average reduction of 0.9% (± 1.8) in HbA1c at the 3rd month. Changes in the lipid profile were also evaluated after three months but reductions in total cholesterol, LDL cholesterol and triglyceride levels were not considered statistically significant.

There was a mean reduction 4.2 kg (± 3) in weight, 1.3 m (± 1.4) in waist circumference and 1.6 kg/m² ($\pm 1,2$) in BMI at the 6th month. There was an average reduction of 0.79% (± 1.7) in HbA1c at the 6th month. On the contrary to the three-month evaluation of lipid profile, the mean reduction on the total cholesterol level was 17.6 mg/dL ($\pm 37,5$), on the LDL cholesterol level was 13.4 mg/dL ($\pm 33,7$) and on the triglyceride level was 25.9 mg/dL ($\pm 65,9$) and these changes were statistically significant.

In Table 4, it is shown whether the mean changes in lipid profiles at the third and sixth months after the use of dapagliflozin are influenced by age, gender, disease duration, hypertension history and using insulin. Mean triglyceride levels decreased by 42.6 mg/dL (± 57) at the end of the third month in patients under 55 years of age which increased by a mean of 2.9 mg/dL (± 52) in patients over 55 years of age. There was no significant effect of age on the triglyceride changes observed at the end of the sixth month. There was no significant effect of patient age on changes in total cholesterol and LDL cholesterol levels in the third and sixth months. Sex, duration of illness, hypertension or insulin treatment did not have a significant effect on total cholesterol, LDL cholesterol and triglyceride changes.

5. Discussion

SGLT-2 is responsible for 90% of the glucose uptake in proximal tubules [9]. Dapagliflozin inhibits the SGLT-2 molecule, reducing plasma sugar independently of insulin release [10]. In this study, we evaluated changes in the lipid profile of patients using dapagliflozin retrospectively. There were a few studies done in the literature with the change of lipid levels which the results were contradictory. In a study by Stephan Matthaei et al., Changes in LDL cholesterol, triglyceride and total cholesterol levels were investigated after 24 weeks of dapagliflozin use. There was an increase in LDL cholesterol and total cholesterol after 24 weeks while a decrease in triglyceride level was observed which was not statistically significant [11]. In the study by Toshiyuki Hayashi et al., the changes observed in the lipid profile of 40 patients who used dapagliflozin were examined after three months. A 2.5% increase in total cholesterol, 0.5% increase in LDL cholesterol and 12% decrease in triglyceride level were observed, but these changes were not statistically significant [12]. At the end of the third and sixth months of Hidekatsu Yanai and colleagues' study, a decrease in LDL cholesterol level was observed despite an increase in triglyceride level. However, these changes were not statistically significant [13]. According to our data, at the end of the third months, a reduction in total cholesterol, LDL cholesterol, and triglyceride levels was detected, but these

Table 2

Change from baseline at third months in lipid profiles.

	0. Month	3. Month	p	0-3 Dif.
Weight (kg)	87,4 (±17,8)	84 (±18,3)	<0,001	-3,3 (±2,5)
BMI (kg/m ²)	33,2 (±6,8)	31,9 (±6,9)	<0,001	-1,3 (±1)
Waist circumference (cm)	106,4 (±15,3)	105,1 (±15,2)	<0,001	-1,3 (±1,3)
HbA1c (%)	8,5 (±1,9)	7,6 (±1)	0,011	-0,9(±1,8)
FPG (mg/dl)	192,7 (±62,6)	151,5 (±73,7)	0,013	-41,1 (±87,1)
PPG (mg/dl)	269 (±79,2)	182,7 (±44,6)	<0,001	-86,3 (±63,1)
T. cholesterol (mg/dl)	217,3 (±43,4)	210,4 (±41,3)	0,32	-6,9 (±38)
LDLc (mg/dl)	134,1 (±41,2)	130 (±35,1)	0,53	-4,09 (±35,9)
Triglyceride (mg/dl)	188,4 (±82,6)	169,3 (±65,2)	0,08	-19 (±58,6)

BMI:Body mass indeks, FPG:Fasting plasma glucose, PPG:postprandial plasma glucose T. cholesterol: total cholesterol, LDLc: Low Density Lipoprotein cholesterol, Dif:Difference.

Table 3

Change from baseline at six months in lipid profiles.

	0. Month	6. Month	p	0-6 Dif.
Weight (kg)	87,4 (±17,8)	83,1(±18,4)	<0,001	-4,2 (±3)
BMI (kg/m ²)	33,2 (±6,8)	31,5 (±7)	<0,001	-1,6 (±1,2)
Waist circumference (cm)	106,4 (±15,3)	105 (±15,3)	<0,001	-1,3 (±1,4)
HbA1c (%)	8,5 (±1,9)	7,7 (±1)	0,018	-0,79 (±1,7)
FPG (mg/dl)	192,7 (±62,6)	150,6 (±3)	0,003	-42,1 (±72,1)
PPG (mg/dl)	269 (±79,2)	194,8 (±78,2)	<0,001	-74,2 (±94,4)
T. cholesterol (mg/dl)	217,3 (±43,4)	199,7 (±32)	0,014	-17,6 (±37,5)
LDLc (mg/dl)	134,1 (41,2)	120,6 (±28,2)	0,034	-13,4 (±33,7)
Triglyceride (mg/dl)	188,4 (±82,6)	162,4 (±58,4)	0,036	-25,9 (±65,9)

BMI:Body mass indeks, FPG:Fasting plasma glucose, PPG:postprandial plasma glucose, T. cholesterol: total cholesterol, LDLc: Low Density Lipoprotein cholesterol, Dif:Difference.

Table 4

Third and sixth month changes of lipid profiles.

		T.kolesterol 0-3.ay	T.kolesterol 0-6.ay	LDLc 0-3.ay	LDLc 0-6.ay	TG 0-3.ay	TG 0-6.ay
Age	<55	-3(±31,4)	-21,8(±38)	4,1(±30)	-13(±34)	-42,6(±57)	-45(±84)
	≥55	-10,5(±44)	-13,7(±37)	-11,8(±39)	-13(±33)	2,9(±52)	-7,5(±36)
	p	0,59	0,56	0,22	0,96	0,02	0,123
Sex	M	-9,4(±48)	-16,4(±46)	-5,9(±49,8)	-12(±42)	-19(±44,7)	-14(±41)
	F	-5,8(±34)	-18(±34,6)	-3,3(±29,8)	-13(±30)	-19(±64,4)	-30(±73)
	p	0,81	0,91	0,86	0,90	0,98	0,54
Duration of type 2 DM (Years)	<10	-1,9(±42)	-17,7(±43)	0,78(±39)	-10(±38)	-19(±64)	-45(±76)
	≥10	-11(±35)	-17,5(±33)	-8(±32,8)	-16(±30)	-18,9(±55)	-9,6(±52)
	p	0,51	0,98	0,5	0,64	0,98	0,13
HT	pos	-6,4(±38)	-9,3(±35)	-5,2(±33)	-8,1(±32)	-4,7(±61,6)	-12(±65)
	neg	-7,5(±39)	-27,7(±39)	-2,7(±39,9)	-19(±35)	-36,5(±51)	-42(±64)
	p	0,93	0,18	0,85	0,34	0,13	0,20
Insulin treatment	pos	-14(±45,8)	-14(±42,7)	-10,5(±47)	-8,9(±38)	-27(±71)	-34(±85)
	neg	-4 (±35,7)	-18,8(±36)	-1,8(±31,7)	-15(±32)	-16(±55)	-22(±59)
	p	0,54	0,77	0,56	0,66	0,66	0,66

HT: Hypertension, M:Male, F:Female, pos:positive, neg:negative, TG:Triglyceride, T. cholesterol: total cholesterol, LDLc: Low Density Lipoprotein cholesterol.

decreases were not statistically significant. At the end of the sixth month, there was decrease in total cholesterol, triglyceride and LDL cholesterol levels and these changes were statistically significant, as opposed to the changes observed in the third month. We investigated the effect of age, sex, duration of diabetes, hypertension history and insulin treatment on changes in lipid profile. It was seen that being below or above the age of 55 had an effect on triglyceride changes observed at the third month but this data was not considered significant. Because it was found that the change in triglyceride observed at the end of the third month was not significant in all patients. Other parameters had no significant effect on the lipid profile.

In our study, it can be said that dapagliflozin positively affected the lipid profile in the long term. However, it should be reminded that the effect of dapagliflozin on the lipid profile is an independent effect of weight loss and glycemic control, and that when different

results are taken into consideration in the literature, more studies are needed to reach the correct data.

6. Conclusion

In conclusion, dapagliflozin therapy offers a new treatment option independent of insulin action in type 2 DM treatment. Dapagliflozin decreases the fasting plasma glucose, post-prandially plasma glucose and HbA1c levels by increasing glucose excretion in the urine. In addition, due to their positive effects on weight and lipid profile, dapagliflozin may be a useful treatment option in the overweight/obese and dyslipidemic diabetic patients.

Conflicts of interest

None to declare.

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