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Original Research Article

The Effect of Dapagliflozin Therapy in Lipid Profile and Cytokine for Diabetic Patients

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Abstract: The cross sectional study was determined the effective of dapagliflozin in lipid profile and cytokine in diabetic patients. The study was performed on 50 patients with diabetic mellitus in age between 40-65 years (22 males and 28 females) in Tikrit city from June 2023 until August 2024. The study was showed the significantly decreased the triglyceride level $p < 0.01$, cholesterol level $p < 0.005$, low density lipoprotein level (LDL) $p < 0.005$ and very low density lipoprotein level (VLDL) $p < 0.005$ and significantly increased high density lipoprotein level (HDL) $p < 0.005$. Potential side effects of the treatment include frequent urination, dizziness, or lightheadedness. When getting up from sitting or lying down, rise slowly to prevent dizziness and lightheadedness, although it could increase the chances of developing genital thrush and urinary tract infections. Also the study explained the significantly decreased the cytokine $p< 0.005$. The aim of the current study has study the effective of dapagliflozin on lipid profile and cytokine.

Keywords: Patients of diabetes mellitus, dapagliflozin tablet 10mg, kit for lipid profile and cytokine.

INTRODUCTION

Diabetes mellitus is a prevalent metabolic condition marked by insufficient insulin secretion and/or action, leading to high blood sugar levels and disruptions in carbohydrate, lipid, and protein metabolism [1].

Lipoprotein abnormalities commonly found in type 2 diabetes, also known as noninsulin-dependent diabetes mellitus, consist of elevated triglycerides and decreased HDL cholesterol in the blood. Furthermore, LDL can be transformed into smaller, potentially more atherogenic lipoproteins known as small dense LDL [2].

Inflammation has been proposed to contribute to diabetes mellitus [3], with the inflammatory response involving acute phase proteins and cytokines potentially influencing the development of diabetes [4]. Elevated levels of inflammatory cytokines like IL-6 [5], IL-17 [6], TGF-β [7], and CRP have been demonstrated in diabetic patients, and these heightened cytokines are significant in the advancement of cardiovascular complications [8].

Acute phase reaction and systemic inflammation are caused by the cytokine TNF-α, which is produced by active macrophages, CD4+ lymphocytes, natural killer cells, neutrophils, mast cells, eosinophils, and neurons [9]. By directly altering the insulin signaling system, TNF-α contributes to insulin resistance, which in turn leads to type 2 diabetes and obesity [10-11]. We conducted a combined analysis of how TNF-α influences the development of vascular damage in diabetic individuals [12]. Elevated levels of TNF-α in the bloodstream have been documented in individuals with diabetes [13]. Elevated blood sugar levels trigger the secretion of TNF-α from monocytes and endothelial cells [14].

Dapagliflozin is a type 2 diabetes medication in tablet form that helps control high blood sugar levels by inhibiting sodium-glucose cotransporter 2 and promoting the removal of glucose from the blood by the kidneys through urine excretion by sodium-glucose co-transporter 2 inhibitor (SGLT-2). The most common adverse effect are female genital mycotic infection, urinary tract infection, and urinary frequency [15].

Dapagliflozin is suitable for patients with uncontrolled blood glucose levels on diet and exercise, and who are unable to tolerate metformin. It can also be employed as a supplement to other antidiabetes drugs, such as insulin, when these medications in combination with exercise and diet are not effectively managing the diabetes [16].

The typical amount of dapagliflozin to be taken is 10mg daily. When using a combination tablet like dapagliflozin with metformin or dapagliflozin with saxagliptin, the dosages might differ [17].

MATERIAL AND METHODS

Observation, prospective study of diabetic patients who received only dapagliflozin 10 mg orally after food were carried out to patients who in Tikrit Teaching Hospital, the work carried from June 2023 to August 2024.

The study has involved 50 patients (22 males and 28 females). This involve patients with diabetes mellitus. These patients take this drug once time daily after food for nine months.

The lipid profile checked by using procedures were performed according to the recommendation of the kit manufacturing company (Randox).

The cytokine is checked by using ELISA methods.

The samples were are taken by vein puncture after 12 hours fasting.

Information assortment included: patients with diabetes mellitus, drugs, lipid profile and cytokine effect.

Quantitative variables are represented as mean ± standard deviation (SD) for the applied mathematical analysis of the information. The student t-test was employed to analyze the quantitative variable.

A P value below 0.05 was considered to be statistically significant.

RESULT

Every participant successfully finished the study. The research aimed to investigate how dapagliflozin 10 mg impacts levels of triglycerides, total cholesterol, LDL-cholesterol, HDL-cholesterol, VLDL, interleukin-6, and tumor necrosis factor (TNF). The effect of the dapagliflozin 10mg daily for nine months after food on lipid profile (triglyceride, cholesterol, low density lipoprotein, very low density lipoprotein and high density lipid profile) is significantly effect. (table 1)

The effect of the dapagliflozin 10mg daily after food on tumor necrosis factor and interleukin-6 which significantly effect. (table 2)

Also, there is appearance some side effect as frequent urination, dizziness, genital thrush and urinary tract infection.

Table 1: Effect the dapagliflozin on the lipid profile after 9 months of treatment

	Normal range	Before treatment	After nine months of treatment
Triglyceride	Less than 150mg/dL	195.34± 64.60	151.52± 99.88*
Cholesterol	Less than 200mg/dL	287.3± 114.53	176.1± 20.89**
LDL	Less than 100mh/dL	134.8± 5.97	92.36± 27.32**
VLDL	2 – 30 mg/dL	34.9± 6.29	10.52± 28.78**
HDL	More than 40mg/dL	30.58± 5.715	44.28± 32.54**

***P < 0.01**

****p < 0.005**

Table 2: Effect the dapagliflozin on the cytokine after 9 months of treatment

	Normal range	Before treatment	After nine months of treatment
TNF-α	0-16 pg/ml	19.986± 6.01	4.074± 0.97**
IL6	5-15 pg/ml	16.986± 0.90	4.44± 1.68**

****p< 0.005**

DISCUSSION

This study found that dapagliflozin medication affected the blood lipid profile by raising HDL levels and decreasing triglycerides, total cholesterol, LDL, and VLDL levels, while increasing HDL levels. Additionally, there was a significant decrease in interleukin-6 and tumor necrosis factor levels.

Diabetes-related atherosclerosis is commonly linked to higher levels of interleukin (IL)-18 and IL-1β due to the activation of NLRP3 inflammation that includes the creation of ROS. Treatment using dapagliflozin can potentially block the ROS-NLRP3 pathway by reducing blood sugar and lipid levels, leading to decreased production of IL-1β and IL-18, and slowing down the advancement of atherosclerosis in aortic tissue [18].

Lenge *et al.*,'s study similarly discovered that administering dapagliflozin for 1 week led to a notable reduction in triglyceride levels in ApoE mice [19]. Min *et al.*, [20] demonstrated that dapagliflozin reduces triglyceride levels and boosts HDL levels.

Dapagliflozin significantly decreased blood TNF-alpha levels in diabetic individuals with coronary artery disease after six months, according to Sato and colleagues' findings [21] of treatment. However, there is no information available on the impact of dapagliflozin on serum TNF-α levels in rabbits. The variations in outcomes could be attributed to the drug being tested on humans instead of rabbits, and the duration of this study being longer than ours. Gaspari and colleagues discovered that treating ApoE adult mice with dapagliflozin for 4 weeks decreased molecular alterations and endothelial cell dysfunction linked to early atherosclerosis [22]. The dysfunction of endothelial cells is a primary factor in the initial stages of atherosclerosis in person with type 2 diabetes. Increased expression of adhesion molecules causes impaired function of endothelial cells and is seen as an early indicator of atherosclerosis development. Dapagliflozin may affect the development and advancement of atherosclerosis in ApoE mice by decreasing endothelial dysfunction, macrophage infiltration, and increasing intercellular cell adhesion molecule-1 expression [23].

CONCLUSIONS

The findings of this study suggest that dapagliflozin could potentially improve atherosclerosis by partially impacting inflammatory and oxidative processes, leading to a decrease in atherosclerotic plaque formation. The research documented a notable improvement in lipid profile and cytokine levels after patients with diabetes mellitus were given dapagliflozin orally.

Dapagliflozin suppressed potent atherogenic LDL- concentration and increased HDL concentration.

However, our study needs further clinical studies to be carried out on large population.

Abbreviations

CRP:	C-reactive protein
DM:	Diabetes mellitus
LDL:	Low density lipoprotein
IL-6:	Interleukin-6
HDL:	High density lipoprotein
NLRP3:	NOD-like receptor family pyrin domain containing 3
ROS:	Reactive oxygen species
SGLT-2:	Sodium glucose cotransporter-2
TNF-α:	Tumor necrosis factor
TGF-β:	Transforming growth factor-beta
VLDL:	Very low density lipoprotein

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