The Effect of Metformin Therapy for Patients with Type 2 Diabetes Mellitus on Serum Lipid Levels

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ABSTRACT

Background: Patients with diabetes mellitus often have dyslipidemia and accelerated atherosclerosis; therefore, effective management of dyslipidemia can lower death and morbidity rates while improving the quality of life for these patients. When used by diabetic patients, lipid-lowering medications like statins can have a number of adverse side effects that worsen the quality of life in addition to providing less-than-ideal results.

Aim of the study: This study aims to investigate how metformin medication affects the blood lipid levels of individuals with type 2 diabetes.

Methods: Forty-five type 2 diabetes patients, ranging in age from thirty to less than sixty, were involved in this study. For two months, patients received 500 mg of metformin orally (Glucomet, Furat Pharmaceutical Industries, Iraq). The total cholesterol, triglyceride, and HDL levels were measured using the Abbott, USA Cholesterol, Triglyceride, and HDL kits. The methods followed the guidelines supplied by the supplier.

Results:The study compared the average levels of serum lipids before and after treatment. The results indicated that there were no significant changes in mean serum cholesterol, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) ($p > 0.05$). However, there was a significant decrease in very low-density lipoprotein (VLDL) ($p < 0.001$) and triglyceride levels ($p < 0.001$), which decreased from 220.69 ± 87.61 mg/dl to 165.21 ± 66.50 mg/dl.

Conclusion: Metformin medicine efficiently and safely reduces blood triglyceride levels in persons with type 2 diabetes mellitus. However, a more extended treatment duration may be necessary to obtain results similar to those for LDL and total cholesterol levels.

Keywords: Diabetes mellitus, HDL, LDL, Cholesterol, Triglyceride

تأثير علاج الميتفورمين على مستويات الدهون في مصل الدم للمرضى الذين يعانون من مرض السكري من النوع الثاني

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الخلاصة

الخلفية: المرضى الذين يعانون من داء السكري غالبا ما يعانون من عسر شحميات الدم ويتسارع لديهم تصلب الشرايين. وبالتالي، فإن العلاج الفعال لاضطراب شحوم الدم يمكن أن يقلل معدلات الوفاة والمعاناة مع تحسين نوعية الحياة لهؤلاء المرضى أيضًا. عند استخدامها من قبل مرضى السكري، يمكن أن يكون للأدوية الخافضة للدهون مثل الستاتينات عدد من الآثار الجانبية السلبية التي تؤدي إلى سوء نوعية الحياة بالإضافة إلى تقديم نتائج أقل من مثالية.

الهدف من الدراسة: تهدف هذه الدراسة إلى معرفة كيفية تأثير دواء الميتفورمين على مستويات الدهون في الدم لدى الأفراد المصابين بداء السكري من النوع الثاني.

طرق البحث: شارك في هذه الدراسة خمسة وأربعون مريضا من مرضى السكري من النوع الثاني، تتراوح أعمارهم بين الثلاثين إلى أقل من ستين عاما. لمدة شهرين، تلقى المرضى ٥٠٠ ملغ من الميتفورمين عن طريق الفم (Glucomet، شركة الفرات للصناعات الدوائية، العراق). تم قياس إجمالي مستويات الكوليسترول والدهون الثلاثية والبروتين الدهني عالي الكثافة (HDL) باستخدام مواد مجهزة من قبل شركة أبوت (الولايات المتحدة الأمريكية)و اتبعت الطرق الإرشادات المقدمة من من قبل الشركة الموردة.

النتائج: قامت الدراسة بمقارنة متوسط مستويات الدهون في الدم قبل وبعد العلاج. أشارت النتائج إلى عدم وجود تغيرات معنوية في متوسط نسبة الكوليسترول في الدم، والبروتين الدهني عالي الكثافة (HDL)، والبروتين الدهني منخفض الكثافة (P >) (LDL 0.05). ومع ذلك، كان هناك انخفاض كبير في مستويات البروتين الدهني منخفض الكثافة (P <0.001) (VLDL) ومستويات الدهون الثلاثية (P <0.001)، والتي انخفضت من ٢٢٠.٦٩ ± ٨٧.٦١ ملغم / ديسيلتر إلى ١٦٥.٢١ ± ٦٦.٥٠ ملغم / ديسيلتر.
الاستنتاجات: دواء الميتفورمين فعال وآمن في خفض مستويات الدهون الثلاثية في الدم لدى الأشخاص المصابين بداء السكري من النوع الثاني، على الرغم من أن مدة العلاج الأطول قد تكون ضرورية للحصول على نتائج مماثلة لمستويات LDL ومستويات الكوليسترول الإجمالية.

الكلمات المفتاحية : مرض السكري، HDL، LDL، الكولسترول، الدهون الثلاثية.

INTRODUCTION

Ischemic heart disease is prevalent among individuals with type 2 diabetes mellitus and contributes significantly to the morbidity and death rates in diabetic patients [1,2]. Ischemia commonly occurs due to the blockage of coronary arteries induced by atherosclerosis [3]. Common risk factors for atherosclerosis include being male, being older, smoking, having high blood pressure, having abnormal levels of lipids in the blood, and other factors [4]. Patients with diabetes mellitus have an increased risk of developing atherosclerosis, and dyslipidemia is frequently observed in diabetic patients. Therefore, effectively treating dyslipidemia can lower the rates of death and disease in patients with diabetes mellitus, and it can also enhance their quality of life [5,6]. Statins, a type of lipid-lowering medication, are commonly prescribed to diabetic patients. However, the effectiveness of these drugs is not always optimal, and they can also cause various adverse effects, negatively impacting the patient's quality of life [7-9].

Several studies have demonstrated that metformin is both efficacious and safe in regulating blood glucose levels and enhancing serum lipid profiles in persons with diabetes [10]. This study aimed to examine the influence of metformin medication on serum lipid levels in persons with type 2 diabetes mellitus.

METHODS OF STUDY

The present study included 45 patients with an age range of 30 to less than 60 years. Those patients were diagnosed with type 2 diabetes mellitus by a specialist physician in the diabetes consultation clinic in the diabetes center at Adiwaniyah Teaching Hospital, Adiwaniyah Province, Iraq. The study is dated back to September 21st, 2023, and extended to March 31st, 2024. The patients should be between 30 and 60 years old. Patients were given metformin (500 mg orally; Glucomet, Furat Pharmaceutical Industries, Iraq) for two months. The study received permission from the institutional review board of the College of Medicine at the University of Al-Qadisiyah. Participants were instructed to provide verbal agreement after thoroughly explaining the objectives and methods of the study.

Total cholesterol, triglyceride, and HDL were measured using (Cholesterol Kit, Triglyceride Kit, andHDL Kit, Abbott, USA), and the procedures were done based on instructions provided by the supplying company.An enzyme-based method in which cholesterol estersarehydrolyzed by esterase enzyme through the process of enzymatic hydrolysis that gives rise to inactive forms, free cholesterols, and fatty acids. Hydrolysis of Triglycerides happens to glycerol and FFA through the action of lipase. Phosphorylation of Glycerol happens then via glycerol kinase (GK) with adenosine triphosphate (ATP) to form glycerol-3-phosphate and an assortment of other metabolites, including NAD. The new Ultra HDL assay can be used for fast and direct detection of serum or plasma from patients in a simplified one-step operation without additional pre-treatment or centrifugation steps.

RESULTS

Table 1 shows the demographic characteristics of the study sample. In this study, men constitute a slightly higher proportion than the female population, with 25 males (55.6%) compared to 20 females (44.4%). Hence, the ratio of males - females is 1.25:1. The mean age of the 45 participants who were registered was 54.13 ±8.58 years, ranging from 35 to 65 years.

Table 1: Demographic characteristics of enrolled diabetic patients

Characteristic	Result
Age (years)	
Mean ±SD	54.13 ±8.58
Range	35 to 65
Sex	
Male, n (%)	25(55.6%)
Female, n (%)	20 (44.4%)
Male: Female ratio	1.25:1

SD: standard deviation

Table 2compares the average serum lipid profile before and after treatment. There were no significant changes in the average levels of serum cholesterol, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) before and after treatment ($p > 0.05$), as shown in figures 1 through 3. However, the treatment did result in a significant decrease in very low-density lipoprotein (VLDL) from 43.91 ±17.39 mg/dl to 33.02 ±13.28 mg/dl ($p <0.001$), as shown in Figure 4. Additionally, there was a significant reduction in triglyceride levels from 220.69 ±87.61 mg/dl to 165.21 ±66.50 mg/dl ($p <0.001$), as shown in figure 5.

Table 2: Comparison of mean serum lipid profile before and after treatment

Characteristic	Before *n* = 45	After *n* = 45	*P*
Cholesterol (mg/dl)			
Mean ±SD	178.63 ±44.79	173.56 ±42.90	0.495 Pa NS
Range	85 - 280	88 - 240	
LDL (mg/dl)			
Mean ±SD	94.36 ±40.41	97.94 ±39.63	0.596 Pa NS
Range	9 -182	8 -163	
HDL (mg/dl)			
Mean ±SD	41.68 ±10.88	40.65 ±7.09	0.477 Pa NS
Range	26 -85	25.72 -61	
VLDL (mg/dl)			
Mean ±SD	43.91 ±17.39	33.02 ±13.28	< 0.001 Pa ***
Range	11.8 - 83	12 -61	
Triglyceride (mg/dl)			
Mean ±SD	220.69 ±87.61	165.21 ±66.50	< 0.001 Pa ***
Range	59 - 415	61.3 - 305	

N: number, SD: standard deviation, Pa: Paired t-test;NS: non-significant, BMI: body mass index,LDL: low-density lipoprotein; HDL: highdensity lipoprotein,VLDL: very low density lipoprotein

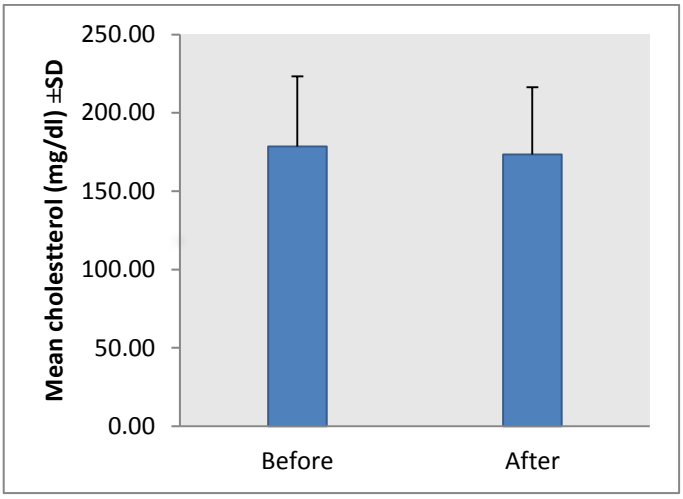

Figure 1: Bar chart showing a comparison of mean cholesterol before and after treatment

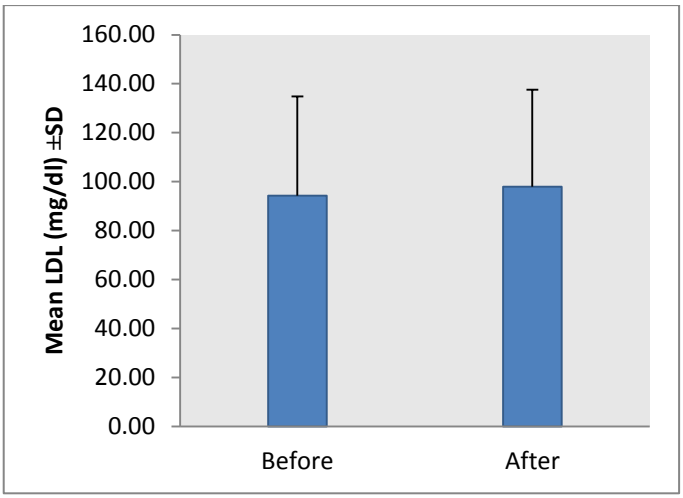

Figure 2: Bar chart showing the comparison of mean LDL before and after treatment

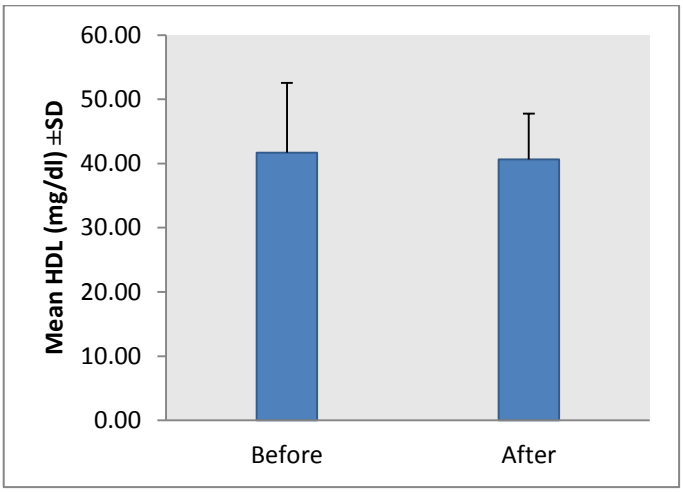

Figure 3: Bar chart showing the comparison of mean HDL before and after treatment

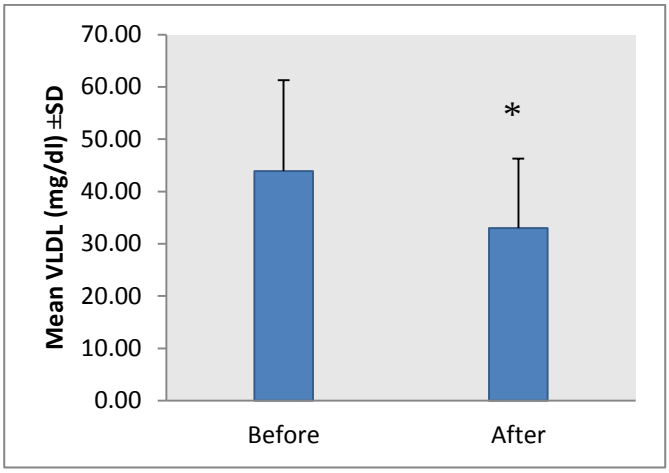

Figure 4: Bar chart showing the comparison of mean VLDL before and after treatment

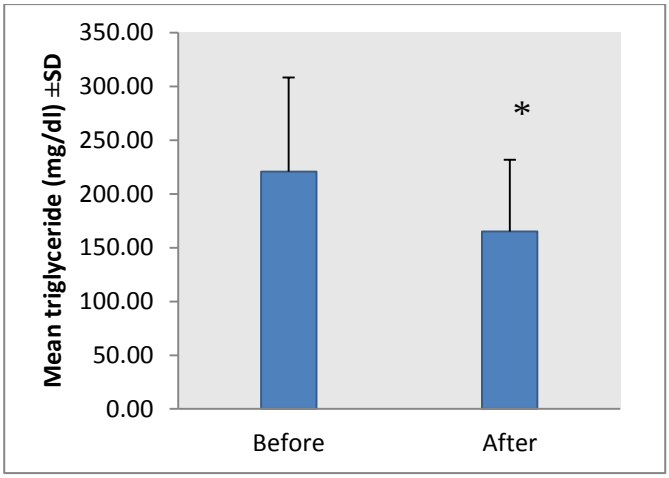

Figure 5: Bar chart showing the comparison of mean triglyceride before and after treatment

DISCUSSION

The current study demonstrates that metformin treatment is linked to a substantial decrease in average serum levels of very low density lipoprotein (VLDL) and triglycerides. However, there are no significant alterations in average serum cholesterol, (HDL), and (LDL).

The study conducted by Lin et al. examined 155 patients over the age of 20 diagnosed with recent-onset T2DM[11]. These patients received metformin monotherapy for at least 12 months and had their serum lipid levels assessed every six months. The study yielded the following results: Following the initiation of metformin treatment, there was a significant decrease in LDL-C values from 111 mg/dL to 102 mg/dL after six months ($P < 0.001$). In addition, the triglyceride (TG) levels decreased from 132 mg/dL to 122 mg/dL after 12 months ($P = 0.046$), and the high-density lipoprotein cholesterol (HDL-C) levels increased from 45.1 mg/dL to 46.9 mg/dL after 12 months ($P = 0.02$).

Therefore, the results of the current investigation are consistent with the findings of Lin et al. [11] about changes in average blood triglyceride levels. However, the two studies have differences in average serum LDL, HDL, and cholesterol levels.However, it is essential to note that the considerable improvements in serum HDL levels described in the study conducted by Lin et al.[11] were observed only after a 12-month treatment period. A 6-month treatment duration did not have a noticeable effect on serum HDL levels. Therefore, based on our analysis, a 3-month time may not be sufficient to observe all the positive effects of metformin in treating dyslipidemia in patients with type 2 diabetes mellitus. This highlights the need for a more extended treatment duration to accomplish these results.

Metformin can reduce disturbances in lipid metabolism in individuals diagnosed with Type 2 Diabetes Mellitus through many pathways [12,13].

Metformin enhances insulin sensitivity, leading to a decrease in the rate of lipolysis. This results in a slowdown in converting free fatty acids into lipoprotein precursors in liver tissue [14]. Metformin lowers blood glucose levels, reducing irreversibly glycated LDL-C levels. This particular type of LDL-C is eliminated with lower efficiency from the body[15]. Furthermore, metformin enhances dyslipidemia by promoting weight reduction in individuals with impaired glucose metabolism [16,17].

Following metformin medication, weight loss is often moderate and mainly attributed to fat reduction rather than an improvement in energy expenditure [18].

The present investigation revealed a somewhat higher proportion of men than females, with a male-to-female ratio of 1.25:1. The participants' ages ranged from 35 to 65 years, with an average age of 54.13 ±8.58 years. Consistent with a previous investigation conducted by Nordström et al. about gender distribution, a higher prevalence of type 2 diabetes mellitus was found in males (14.6%) compared to females (9.1%)[19]. Li et al. also provided evidence to corroborate this finding[20]. In contrast, Li et al. discovered that among the 12,766 diabetes patients they examined, there were 5963 males and 6803 females, suggesting a somewhat more significant proportion of female diabetic patients[21].

The hypothesis proposed to explain the higher prevalence of type 2 diabetes mellitus in males, as opposed to women, in this study can be linked to the more significant occurrence of central obesity in men. This results in a more considerable amount of visceral fat in men compared to women. Visceral fat accumulation has been associated with insulin resistance and an increased vulnerability to type 2 diabetes mellitus [22,23].

In their study, Carrillo-Larco et al. examined a cohort of 8695 individuals diagnosed with type 2 diabetes mellitus and determined that the mean age was 45 years[24]. The mean age reported by Carrillo-Larco et al.[24] seems lower than the age recorded in the ongoing study (54.13 years). However, it is essential to note that not all participants in this research are newly diagnosed, as a significant proportion had been diagnosed with type 2 diabetes mellitus many years before their enrollment. A separate research study examined 3525 patients from various countries in the Middle East and found that the average age was 54.3 ± 10.8 years, which is similar to the age reported in the current study.

CONCLUSION

Short-term treatment with metformin is efficient and safe in reducing serum triglyceride in patients with type 2 diabetes mellitus; however, a longer duration may be needed to see the same effect concerning LDL and total cholesterol levels.

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