

Effect of Metformin on Weight and Biochemical Indices in over Weight and Obese Diabetics

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Abstract

An effect of metformin on weight and biochemical parameter for 6 month or longer is extensively studied while the effect of only 3 months is not fully elaborated. In our retrospective study we collect and analyze data for the effect of metformin (3 months) on obese newly diagnosed diabetic on diet control (Mediterranean diet with reduce total calories intake) following a registered Nutritionist at Elkodes clinic. We include data of all overweight and obese newly diagnosed diabetics before and after 3 months period of starting metformin in addition to diet control. Patients on anti-lipid or weight reduction therapy and patient with known liver or renal disease were excluded. Paired T test was used. The mean weight, T cholesterol, Triglyceride, LDL-C and as expected HbA1c (72.04 Kg, 182.4 mg/dl, 135 mg/dl, 85.6 mg/dl, 6.1) was significantly lower after metformin compared to before therapy (83.6 Kg, 208.5 mg/dl, 169mg/dl, 113mg/dl, 7.9) respectively. Renal and liver functions were not statistically different. Our study shows that metformin can have significant favorable effect on weight and lipid profile even for (3 months) use without effect on liver function. Most previous evidence demonstrates the effect of metformin after 6 months or longer.

Keywords: Metformin effect; Obesity; Diabetes.

Introduction

Metformin is an orally administered drug is recommended as first-line pharmacological treatment for type 2 diabetes (T2D) in almost all diabetic and endocrine scientific society guidelines [1-2]. Previously known that the main anti hyperglycemia effect of metformin through inhibition of the hepatic glucose output but recently there is increasing evidence that the primary effect of metformin may resides in the human gut [3-4]. Fineman and their colleagues show clearly that metformin effect on the glycemic control through the gut may be stronger than its effect systemically through its effect on hepatic glucose output and they develop whets called delayed release metformin Met DR tablets [4].

The major advantages of metformin are improvement of peripheral insulin sensitivity, controlling hyperglycemia with low risk of hypoglycemia, and without inducing weight gain, actually there is evidence of promoting weight loss and cardiovascular safety [5-7]. Similarly, there is growing body of evidence that metformin

is an antioxidant that reduce cancer risk [8].

Metformin induces modest weight loss most likely through a loss of adipose tissue [9]. A systematic review conducted by Alicia R Desilets and their colleagues in 2008 conclude that 'The weight loss effects of metformin in overweight or obese adults and adolescents without diabetes appear promising; however, trials have been limited by small patient populations and weak design. Metformin may also have a positive effect on metabolic parameters such as waist circumference, fasting insulin and glucose levels and triglycerides' [10].

A recent study demonstrates that metformin may also reduce Lipid through an AMP-activated protein kinase pathway [11]. However, most studies have review the effect of 6 months or more of metformin on weight and lipid profile while the short term effect for 3 months was not extensively studied, that's why our study focus on this reasonably deficient area of metformin effect.

Patients and Method

Study design

A retrospective study involving data from the file notes of registered nutritionist from 2012 -2015 at Ekods clinic. We include data of all overweight and obese newly diagnosed diabetics before and after 3 months period of starting metformin in addition to diet control.

Exclusion criteria

Patients on anti-lipid or weight reduction therapy and patient with known liver or renal disease were excluded.

Data collection

Weight, total cholesterol (TC), Triglyceride (TG), Low Density lipoprotein-cholesterol (LDL-C), Renal function test (RFT), Liver function test (LFT) and HbA1c before and after 3 months of metformin was collected from the file notes in addition to demographic data.

Data Analysis

The data was analyzed using Statistical package for the social science (SPSS) version 21, paired T test was used to detect the difference in the weight and biochemical indices (T cholesterol, Triglyceride, LDL-C, RFT, LFT and HbA1c) before and after starting metformin. Pearson correlation was used to correlate the dose of metformin and these variables.

Results

Out of all data files searched only 110 patients they fill full the inclusion and exclusion criteria. Eighty six were females (78.1%) and twenty four males (21.8%) [Figure1].

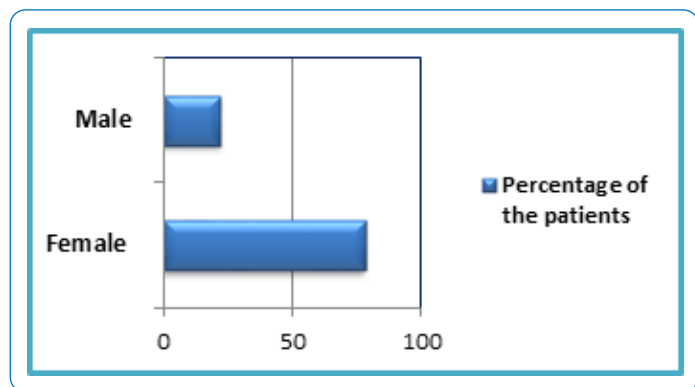


Figure 1: The percentage of the patients in the sample according to gender

Table 1: The mean age of the patients was 37.2 +/- 8.5SD and the range was from (19-58) years

	Sex of the patient	Age of the patients
Valid	110	110
Missing	0	0
Mean		37.2
Median		37.5
Std. Deviation		8.54

A total of 101 were on low dose metformin (500mg /d) and nine patients on moderate dose (1000mg/d) [Figure 2].

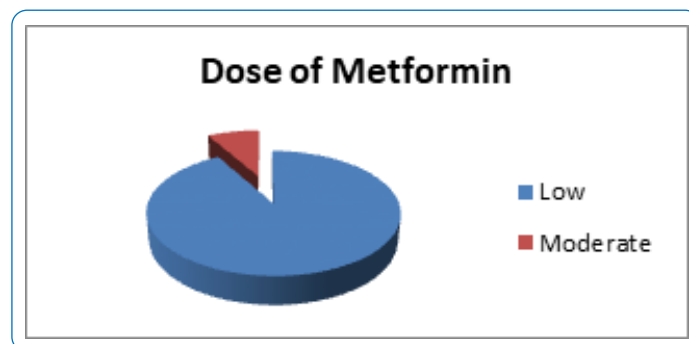


Figure 2: The total daily dose of Metformin in the study sample

There were statistically significant reduction of weight and metabolic parameters after 3 months of metformin therapy as compare to before therapy, weight (83.6 +/- 10.4, 72 +/-9.1 , p value=.000) , total cholesterol (208.5 +/- 49.7, 182.4 +/-40.85 , p value=.000) , LDL -cholesterol (113.3 +/- 31.49 , 85.7 +/- 23.2 (p value=.000) , Triglyceride TG (169.1+/- 78.9 , 135 +/- 52.5, p value=.000) and as expected HbA1c (7.9 +/- 1.2, 6.1 +/- 1.4, p value=.000).

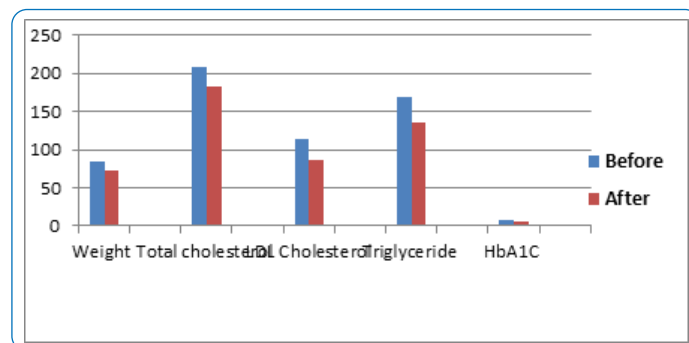


Figure 3: The mean level of the weight and biochemical indices before and after 3 months of metformin therapy

While there were no statistically significant difference before and after 3 month of metformin therapy in the serum creatinine (0.55+/- 0 .2, 0 .51 +/- 0.2, p value =0 .28), liver enzymes, AST (20.2 +/- 6.5, 19.8+/-7.65, p value = 0.693), ALT (19.95 +/- 7.5, 20.1+/- 6.6, p value=0.835).

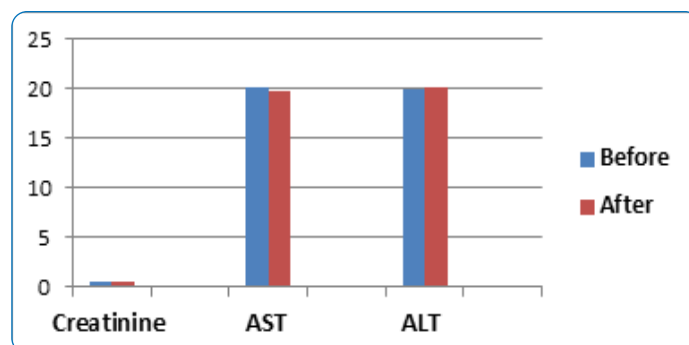


Figure 4: The mean level of Renal and liver function before and after 3 month of metformin therapy

The mean ALT/AST Ratio was slightly increased after metformin therapy (1.2+/-0.7 SD) than before therapy (1.1+/- 0.64 SD) [Table 2].

Table 2: ALT /AST ratio before and after metformin therapy

	N	Minimum	Maximum	Mean	Std. Deviation
ALT/AST ratio before metformin therapy	110	.20	4.30	1.1167	.64274
ALT/AST ratio after metformin therapy	110	.24	4.50	1.2162	.72011

Table 3: Significance of ALT/AST ratio before and after metformin therapy

Paired Differences				t	df	Sig. (2-tailed)	
Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
			Lower	Upper			
-.09945	1.26074	.12021	4.50		-.827	109	.410

In our study there was no significant correlation of weight and biochemical indices (T cholesterol, LDL-C, TG, AST, ALT, creatinine) with dose of metformin used while HbA1 C was significantly correlated with the dose (Pearson's R = 0.231, p value= 0.015). But the limitation of result of correlation that most of the patients were on low dose metformin and small percentage on moderate dose and no patient on high dose.

Discussion

Our study demonstrate significant reduction in weight of the patients on use of metformin for 3 months (83.6 +/- 10.4, 72 +/-9.1, p value=.000). This is in concordance with result of Szu Han Lin, et al. (2018) which they found that mean body weight changed from 69 kilograms to 68.3 kilograms (p = 0:01) [12]. However, this achieved on longer time of treatment (12 months period) than our study.

Seifarth and their colleagues (2013) evaluate the effectiveness of high dose metformin on weight in 154 obese non diabetics over 6 month's period. They found that the mean weight loss in the metformin treated group was 5.8 ± 7.0 kg (5.6 ± 6.5%). Untreated controls gained 0.8 ± 3.5 kg (0.8 ± 3.7%) on average. Patients with severe insulin resistance lost significantly more weight as compared to insulin sensitive patients. The percentage of weight loss was independent of age, sex or BMI. [13].

The effect of metformin on lipids was shown in a study of Szu Han Lin, et al (2018) which conclude that after initiating metformin therapy, LDL-C was significantly reduced from 111 mg/dl to 102 mg/dL (p<0:001), TG was reduced from 132 mg/dl to 122 mg/dL (p =0:046), HDL-C increased from 45.1 mg/dL to 46.9 mg/dL (p =0:02) and mean HbA1c was reduced from 8% to 6.47% (p <0:001) at 6 months to 12 months [12]. These finding are comparable to our finding which shows that Total cholesterol was significantly reduced from (208.5 mg/dl to 182.4 mg/dl , p value=.000) , LDL -cholesterol (113.3 mg/dl to 85.7 mg/dl , p value = .000) , Triglyceride TG (169.1 mg/dl to 135 mg/dl , p value=.000) and as expected HbA1c (7.9 +/- 1.2 , 6.1 +/- 1.4 , p value=.000). But what interesting in our finding that these changes in weight and lipid profile was seen after just 3 months of low or moderate dose of metformin. The existing evidence that hyper triglyceridemia and diminished HDL-C require a longer therapeutic duration to counteract than lowering LDL-C which usually 6-12 months duration is contradicted by our finding which support the rationale that even three month of metformin therapy can lead to significant triglyceride changes [14].

Conclusion

The study shows that metformin can have significant favorable effect on weight and lipid profile even on for (3 months) use. Most previous evidence demonstrates the effect of metformin after 6 months or longer.

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