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Research Article

Metformin Used for Weight Loss by Non-Diabetic Sudanese Females

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Abstract

Metformin, a principle Biguanide, is the main anti-diabetic agent for the treatment of T2DM. It reduces the insulin resistance associated with T2 DM. In addition, obesity, which is found to have a similar pathogenesis may be affected by treatment with Metformin. Young obese non-diabetic females have taken an interest in taking Metformin over-the-counter to lose weight.

Here we studied the practice of using Metformin for weight loss. We performed a cross-sectional study on 50 women, selected randomly at Khartoum State between November to December 2017. All of whom were females and 37.3% more than 30 years old. The majority had a BMI of 35 kg/m^2.

Fifty-eight percent were not married, (28%) and (4%) were pharmacists and physicians respectively and 39.2% used only 500 mg of Metformin once a day. Ninety percent had abdominal disturbance, 58.8% stopped Metformin use because of side effects, 64.7% obtained metformin from the pharmacy as over the counter (OTC) medicines. Thirty percent obtained the information about metformin use from the social media or their friends, 58.8% observed weight loss by more than 5 kg. Fifty-four point nine percent and fifty-eight point eight percent had been on diet and exercise programs respectively, 64.7% were satisfied with their result. There were significant associations between weight reduction with, dose used, diet and exercise.

We conclude that women who used Metformin over the counter had a good experience with it especially when combined with diet and exercise.

Keywords: *Metformin; Obesity; Weight Loss; Insulin Resistance*

Introduction and Literature Review

Background

Metformin hydrochloride is an oral anti-diabetic drug used in the management of type 2 diabetes. Metformin hydrochloride (N, N-dimethy limidodicarbonimidic diamide hydrochloride) is not chemically or pharmacologically related to any other classes of oral anti-diabetic.

Metformin is the first-line medication for the treatment of type 2 diabetes, particularly in people who are overweight. It is also used in the treatment of polycystic ovary syndrome. Evidence suggests metformin may prevent the cardiovascular disease and cancer complications of diabetes. It is not associated with weight gain and is taken by mouth [1].

Metformin is generally well tolerated. Common side effects include diarrhea, nausea and abdominal pain. It has a low risk of causing hypoglycemia. Lactic acidosis is a concern if the drug is prescribed inappropriately and in overly large doses. It should not be used in those with significant liver disease or kidney problems. While no clear harm comes from use during pregnancy, insulin is generally preferred for gestational diabetes. Metformin is in the biguanide class. It works by decreasing glucose production by the liver and increasing the insulin sensitivity of body tissues.

Medical uses

Metformin is primarily used for type 2 diabetes, but is increasingly being used in polycystic ovary syndrome due to the linkage between these two conditions. Outcomes appear to be improved even in those with some degree of kidney disease, heart failure, or liver problems [2,3].

Type 2 diabetes: The American Diabetes Association and the American College of Physicians each recommend metformin as a first-line agent to treat type 2 diabetes [4].

Prediabetes: Metformin treatment of people at a prediabetes stage of risk for type 2 diabetes may decrease their chances of developing the disease, although intensive physical exercise and dieting work significantly better for this purpose. In a large U.S. study known as the Diabetes Prevention Program, participants were divided into groups and given either placebo, metformin, or lifestyle intervention and followed for an average of three years [5].

The incidence of diabetes was 58% lower in the lifestyle group and 31% lower in individuals given metformin.

Among younger people with a higher body mass index, lifestyle modification was no more effective than metformin, and for older individuals with a lower body mass index, metformin was no better than placebo in preventing diabetes.

After ten years, the incidence of diabetes was 34% lower in the group of participants given diet and exercise and 18% lower in those given metformin.

Polycystic ovary syndrome: Anti-diabetic therapy has been proposed as a treatment for polycystic ovary syndrome (PCOS), a condition frequently associated with insulin resistance, since the late 1980s. The use of metformin in PCOS was first reported in 1994, in a small study conducted at the University of the Andes, Venezuela [6].

Female infertility: A systematic review of four head-to-head comparative trials of metformin and clomifene found them equally effective for infertility. Four positive studies of metformin were in women not responding to clomifene, while the population in the negative studies was drug-naive or uncontrolled for the previous treatment. Metformin should be used as a second-line drug if clomifene treatment fails [7].

Gestational diabetes: Several observational studies and randomized, controlled trials found metformin to be as effective and safe as insulin for the management of gestational diabetes. Nonetheless, several concerns were raised and evidence on the long-term safety of metformin for both mother and child is lacking [8,9].

Women with gestational diabetes treated with metformin have less weight gain during pregnancy than those treated with insulin. Babies born to women treated with metformin have been found to develop less visceral fat, making them less prone to insulin resistance in later life [8].

Contraindications

Metformin is contraindicated in people with any condition that could increase the risk of lactic acidosis, including kidney disorders

(arbitrarily defined as creatinine levels over 150 μmol/l (1.7 mg/dl), lung disease and liver disease. Heart failure, in particular, unstable or acute congestive heart failure, increases the risk of lactic acidosis with metformin [10]. A 2007 systematic review of controlled trials, however, suggested metformin is the only antidiabetic drug not associated with any measurable harm in people with heart failure, and it may reduce mortality in comparison with other antidiabetic agents, also contraindicated in alcoholic patients and sever infection [11].

Adverse effects

Gastrointestinal

The most common adverse effect of metformin is gastrointestinal irritation, including diarrhea, cramps, nausea, vomiting and increased flatulence; metformin is more commonly associated with gastrointestinal side effects than most other antidiabetic drugs. This can often be avoided by beginning at a low dose (1.0 to 1.7 grams per day) and increasing the dose gradually but even with low doses 5% of people may be unable to tolerate metformin. Use of slow- or extended-release preparations may improve tolerability [12].

Hypoglycemia in metformin

Metformin does not usually cause low hypoglycemia. Low blood sugar may occur if it is prescribed with other diabetes medications.

In a study, on the risk of hypoglycemia following intensification of metformin treatment with insulin versus sulfonylurea by Christianne L. Roumie, published in 2016, they found that the addition of insulin was associated with a higher risk of hypoglycemia than the addition of sulfonylurea [13].

Lower the amount of vitamin B-12

When metformin was used for a long time, it could lower the amount of vitamin B-12 in the body too much. So, B-12 level should be checked, especially if have anemia or nerve damage in feet or hands (peripheral neuropathy) were found [15].

Metformin and obesity

Obesity has become a major health problem with the introduction of unhealthy food habits. It is a risk factor for many chronic diseases and is known for its role in metabolic syndrome, which can lead to type 2 diabetes (T2D) as well as increased risk for cardiovascular disease [16].

Other factors such as sedentary lifestyle, environmental, cultural and genesity can play a role in becoming overweight or obese.

The best ways to quantify obesity is by anthropometric measures of BMI that is the weight in Kg divided by the height^2 in meters and the waist circumference.

The best way is to classify a BMI of 25 - 29.9 as overweight, 30 - 34.9 grade I obese, 35 - 39.9 grade II obese and > 40 grade III.

A BMI above 30 is considered a high risk for complications.

Obesity is associated with an increased risk for T2Dm, hypertension, dyslipidemia, non-alcoholic fatty liver, obstructive sleep apnea, degenerative joint disease and some malignancies.

There are many options to cure obesity, lifestyle modification, a spectrum of medications and recently bariatric surgery has given promising results.

The following table may assist in decision making (Table 1).

Metformin is not FDA approved for treatment of obesity. But some authors have investigated its use with awarding results.

Treatment	BMI (Kg/m^2)				
	25 - 26.9	27 - 29.9	30 - 34.9	35 - 39.9	=/> 40
Life-style modification	With comorbidities	With comorbidities	+	+	+
Pharmacotherapy	x	With comorbidities	+	+	+
Bariatric surgery	x	x	x	With comorbidities	+

Table 1

The effect of metformin on weight loss

Metformin works basically on the insulin receptors improving insulin resistance. Besides its beneficial effects on weight loss in T2D and possibly in polycystic ovary syndrome (PCOS) it has shown a similar effect on obesity without diabetes.

The mechanism of action for metformin is unique compared with other antihyperglycemic agents. Metformin decreases the production of glucose in the liver, decreases the absorption of glucose in the intestine, and improves insulin sensitivity through increasing muscle glucose uptake and use. Metformin induces weight loss most likely through a loss of adipose tissue rather than a change in energy expenditure, as is seen with exercise [17-20].

The effects of metformin on body weight are variable between patient populations [5]. It is clear, however, that metformin does not increase body weight, in contrast to other oral anti-diabetic agents, and may help to limit the weight gain associated with insulin- or sulphonylurea-based regimens. There is no compelling evidence for the use of metformin to control body weight in nondiabetic populations, although other benefits in terms of a reduced risk of diabetes.

Finally, the evidence for using metformin as treatment of overweight or obesity in adults who have no diabetes mellitus or polycystic ovary syndrome is insufficient, but all have shown a modest and satisfactory reduction in weight.

Justification

Obese ladies who have tried diet and exercise and failed to maintain weight loss, want quick and easy methods to lose weight. It is human nature to try and find an easy solution.

Objectives of the Study

The main objectives were to assess the effect of Metformin used for weight loss by non-diabetic, obese Sudanese females. We also looked into the source of knowledge and their satisfaction with the results as well as the occurrence of side-effects.

Methods

This was a non interventional, descriptive cross sectional study conducted during period from November to December 2017, in Khartoum State. The population included in the study were young women from students in National Ribat University, Faculty of Pharmacy. Khartoum University students in all medical fields and 2 Gymnastic centers in Khartoum. As well, we interviewed pharmacists working in more than 10 pharmacies. We included young women who used Metformin for weight loss and excluded those with diabetes or poly-cystic ovarian syndrome or on anti-psychotic medication.

Data collected using questionnaire sheets which included demographic data and questions to study the practice of off label use of metformin by young women.

Data analysis was performed using Chi-square test to test significant differences between variables. The data was analyzed using Statistical Package for Social Sciences (SPSS version 24) and Microsoft office excel program. P-value ≤ 0.05 was considered significant.

Results

We studied 50 young females mostly unmarried. The majority were students (68%) and 66% obese, a BMI of > 30. The majority, 68.6% used Metformin for an average of 1 - 12 months. Ninety percent had abdominal disturbances and half of them stopped the medication (Table 2).

Variable			
	18 - 25	26 - 30	> 30
Age	27.4%	35.3%	37.3%
Marital status	Yes	No	
	42%	58%	
Occupation	Physician	Pharmacist	Student
	4%	28%	68%
BMI	25 - 30	> 30	
	34%	66%	
Duration of Metformin use	< 1 month	1 - 12 months	> 12 months
	19.6%	68.6%	11.8%
Abdomen disturbance	Yes	No	
	90%	10%	
Stopped Metformin	Yes	No	
	58.8%	41.2%	

Table 2

Most of females (39.2%) used only 500 mg of metformin per day, while fewer took 1 gm a day while only a minority took more than 1 gm (Figure 1).

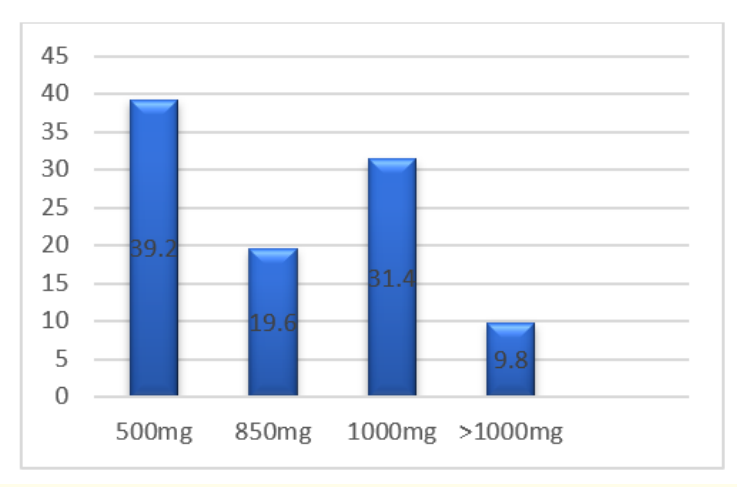

Figure 1: *Distribution of females according to dose of Metformin used.*

Majority of females 64.7% obtained metformin from the pharmacy as over the counter (OTC) medicines (Figure 2).

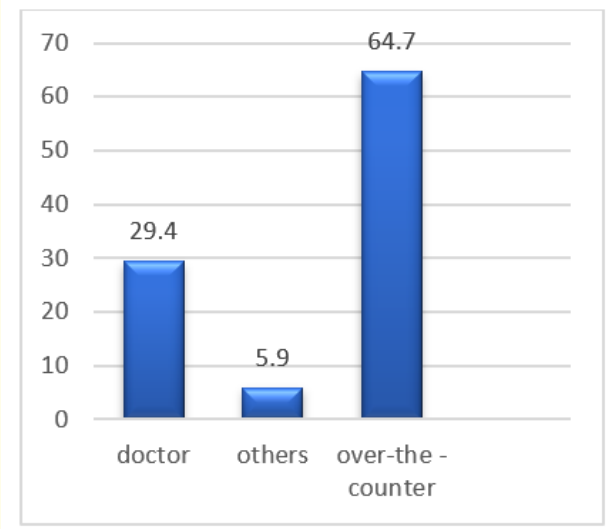

Figure 2: *Distribution of females according to prescriber of metformin.*

Most females (30%) obtained the information about metformin use for obesity from social media or their friends (Figure 3).

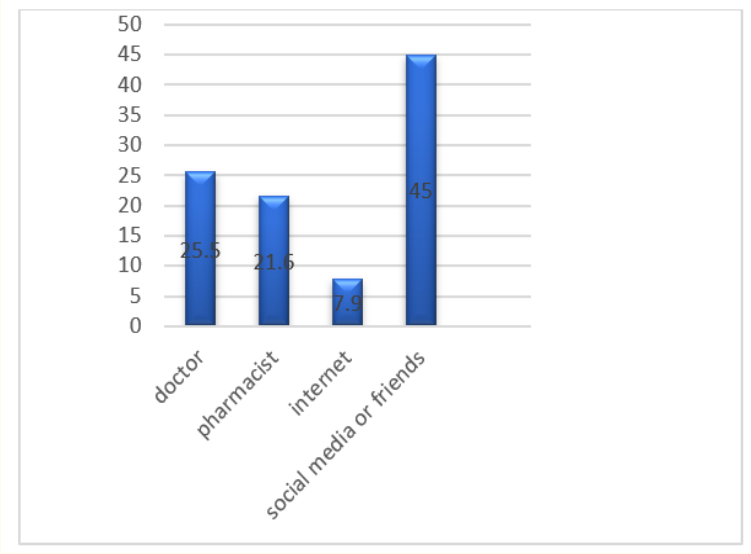

Figure 3: *Distribution of females according to source of information.*

Weight reduction

The majority of females (41.2%) noted a minimum weight reduction of 1 - 5 kg, and 27.4% achieved more than 10 kg weight loss. The average weight before Metformin use was 90 ± 22.5 kg and after Metformin use was 80.5 ± 20 kg, the average weight reduction was 10.7 ± 15 (Figure 4).

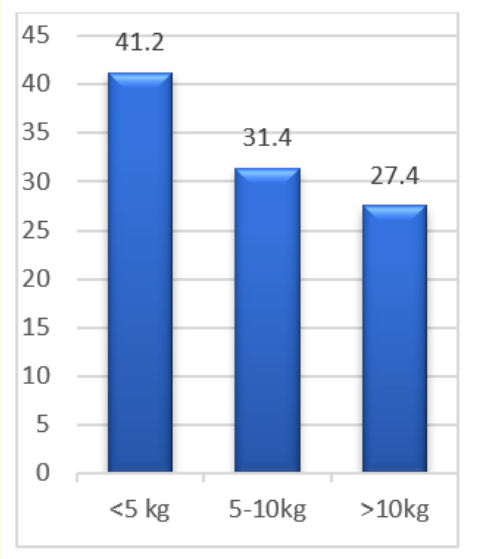

Figure 4: *Distribution of females according to weight reduction.*

Most of females (54.9%, 58.8%) were on diet and exercise program respectively (Figure 5).

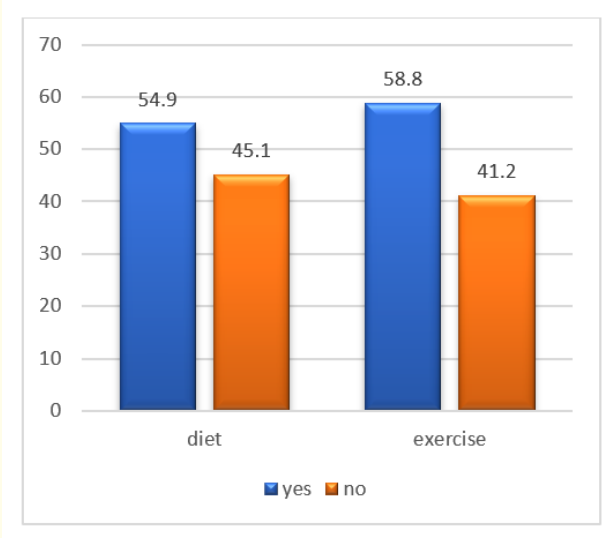

Figure 5: *Distribution of females study according to other method for weight reduction.*

Most of females 66.7% were satisfied from their result but 51% of them didn't achieve their result, also 51% of them would not advise their friend to use metformin for weight loss (Figure 6).

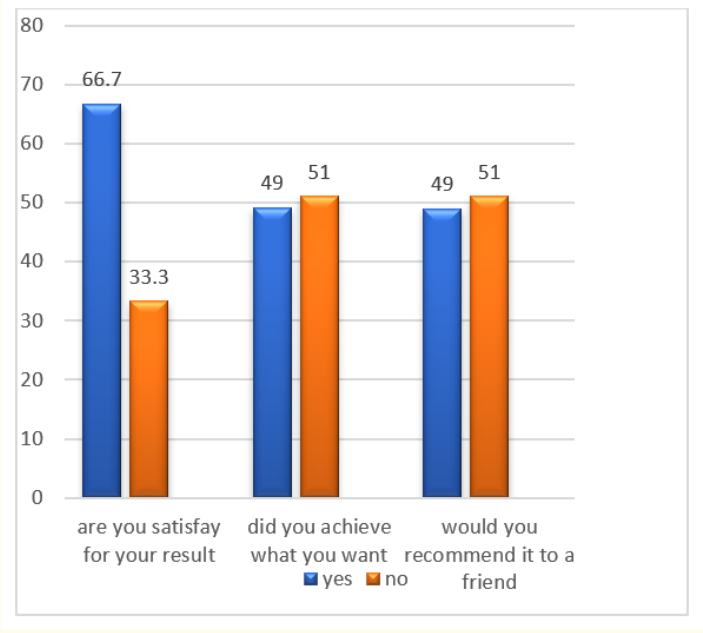

Figure 6: *Distribution of females according to their attitude toward metformin use.*

Associations between weight reduction and other variable

Chi-square correlation test was made between weight reduction and other variable. The result showed that depending on p-value (P-value < 0.05) there were significant associations between weight reduction with age, marital status, duration of use, dose, diet, exercise and satisfaction (Table 3).

Variables	p-value
Age	0.000
Marital status	0.000
Duration of use	0.001
Dose used	0.000
Type of prescriber	0.811
Weight before	0.693
Weight after	0.604
Use diet	0.000
Exercise	0.022
Complications	0.105
Satisfaction	0.000

Table 3: *Associations between weight reduction and other variable.*
**p-value < 0.05 indicated significant associations between variables.*

Discussion

In this study, 58.8% of females reduced their weight by more than 5 kg. The average weight before metformin use was 90 ± 22.5 kg and after metformin use was 80.5 ± 20 kg, the average of weight reduction was 10.7 ± 15, regardless of duration, dose and other weight reducing techniques.

Seifarth C, Schehler B, Schneider HJ, studied the effectiveness of metformin on weight loss in non-diabetic individuals with obesity. They examined the effectiveness of metformin as a weight reducing drug in obese and overweight patients with regard to their degree of insulin resistance. 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. The study concluded that Metformin is an effective drug to reduce weight in a naturalistic outpatient setting in insulin sensitive and insulin resistant overweight and obese patients [20].

Nine out of fifty-seven clinical trials that studied the effect of Metformin on weight reduction, met the criteria for validity assessment. Four studies used the parameter of waist-to-hip ratio, 3 studies included BMI, and 8 used weight. Two of the 9 studies showed a small reduction in WHR. The study concluded that insufficient evidence exists for the use of metformin as treatment of overweight or obese adults who do not have diabetes mellitus or polycystic ovary syndrome. Further studies are needed to answer this clinical question [22].

In this study it was noted that 28% of females were Pharmacists and 4% were physicians while the rest were educated housewives and Gym attendants. This reflects the ease of getting the medication and the need for awareness.

As regards to the side effect and complications of Metformin, in this study the majority of females had abdominal disturbance. This can be explained by the fact that the dose was not taken gradually but started by a high dose so as to lose weight in a short period.

Fujita, Yoshihito; Inagaki, Nobuya (2017) [13]. Reported that gastrointestinal upset can cause severe discomfort, most commonly when metformin is first administered, or when the dose is increased. The discomfort can often be avoided by beginning at a low dose (1.0 to 1.7 grams per day) and increasing the dose gradually but even with low doses 5% of people may be unable to tolerate metformin. Use of slow- or extended-release preparations may improve tolerability.

Most of females using Metformin, 64.7% were satisfied with their result, but 51% of them did not achieve their target. Another 51% of females would advise their friends to use metformin for weight loss because they had a positive experience with it. It is important to note that the differences in confounding factors, endocrine problems, age-related issues, BMI, basal metabolic rate, insulin resistance and physical activity may have led to this result.

Conclusion

Metformin can be used by young non-diabetic obese females for weight loss. Better results can be achieved when combined with diet and exercise. Side effects can be easily overcome by building up the dose gradually.

Authors Contribution

The main author, Dr. Sulaf, drafted the main idea, proposal and questionnaire. The second author, Dr. Miyada, participated in the literature review and results. Dr. Sulaf did the scientific writing and final editing. Both authors reviewed the manuscript and approved the final version.

Conflict of Interest

None of the authors have any conflict of interest, nor advertising for this particular oral antidiabetic medication.

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