EFFECT OF DIFFERENT DOSES OF METFORMIN TABLETS ON METABOLIC SYNDROME COMPONENTS IN WOMEN WITH TYPE 2 DIABETES MELLITUS IN GORGAN (SOUTH EAST OF CASPIAN SEA)

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Studies on oral antihyperglycemic drugs have been shown in some studies to help and treat type 2 diabetic patients. The present study was designed to evaluate and compare the effect of different doses of metformin tablets on metabolic syndrome components in type 2 diabetic women in Gorgan, South East of Caspian Sea. Forty type 2 diabetic patients received 500 mg/day and 1000 mg/day metformin tablets for 12 months and forty healthy women were included in this study. The ATP III criteria were used to determine metabolic syndrome components, and lipid profiles, HbA1c and insulin were measured. Significant differences were found between blood sugar, triglycerides, high-density lipoprotein (HDL)-cholesterol, hemoglobin A1c (HbA1c) and insulin of the patients received 500 mg/day and 1000 mg/day metformin monotherapy. The blood sugar, triglycerides and insulin were significantly lower in patients received 500 and 1000 mg/day metformin than control groups. In both groups, HDL-cholesterol was higher than control groups, but HbA1c was significantly higher and lower in patients received 500 and 1000 mg/day metformin than control groups, respectively. In both study groups, positive significant correlation was found between blood glucose and HbA1c and, blood glucose and triglyceride levels. Our study showed the efficacy of the 1000 mg/day metformin monotherapy on better control of blood sugar, HbA1c, triglyceride and HDL-cholesterol levels, but Metformin had no effect on waist circumference and blood pressure. Treatment with this dose of metformin may be more beneficial for type 2 diabetic patients than those other doses.

INTRODUCTION

The prevalence of diabetes mellitus (DM) was estimated to be 4.4% worldwide in 2030⁴. Diabetes mellitus (DM) is one of the most important causes of mortality worldwide. The diabetes mellitus can cause some diseases such as blindness, kidney failure, heart attacks, and stroke and lower-limb amputation⁵. The prevalence of diabetic people has increased and its prevalence is still rising⁶,⁷. In diabetic people, especially type 2 diabetic people, lacking of glycemic control can affect blood vessels and nerves, progression of neuropathies, micro-and macro-vascular complications and premature death⁸. Metabolic syndrome (MetS), is a cluster of some factors such as abdominal obesity, elevated blood pressure, dyslipidemia and dysglycemia⁹. These are an important risk factor for DM. Some studies have shown that MetS is predictor of DM incident⁵,⁷. However, the clinical effect of MetS is not exactly cleared.
According to the American Diabetes Association and the European Association for the Study of Diabetes, there is an association between MetS and DM due to impaired fasting glucose or impaired glucose tolerance. The Diabetes Prevention Program (DPP) revealed that the risk of developing diabetes was decreased 58% by intensive lifestyle and 31% by metformin interventions in groups with IGT compared with control groups. The DPP provided a data that it is useful to assess the associations of MetS and its components and their alterations with the development of diabetes. According to the UK Prospective Diabetes Study (UKPDS), metformin is an effective drug to control the blood glucose levels of obese type 2 diabetic patients. It has been demonstrated that metformin is an effective drug for non-obese diabetic subjects in a short period of the observation, usually less than one year. Studies have shown that there is an association between metabolic syndrome and a high risk of coronary heart disease and premature mortality. It is reported that metabolic syndrome like diabetes mellitus causes microvascular complications in type 2 diabetic patients. Studies have indicated that 70-80% diabetic people are shown metabolic syndrome. Metformin is a drug has been approved by the Food and Drug Administration for the treatment of type 2 diabetic patients (T2DM). Metformin is as an effective drug that it differs in several respects. There are a number of factors which may make differences in anti-diabetic drug response in different population, such as age, sex, disease, drug and food interactions, co-morbidity, and genetic factors. Metformin may decrease insulin resistance, weight loss and lactic acidosis which are the most serious side effect of metformin. Studies on oral anti-hyperglycemic drugs have been shown in some studies, but the knowledge is not enough for physicians to help and treat T2DM patients. Type 2 diabetic patients treated with 500 mg and 1000 mg per day metformin may be involved in the pathogenesis of the metabolic syndrome. The effects of different doses of this drug on the metabolic syndrome components are exactly unclear. The alterations of metabolic syndrome components may different in different ethnic groups. Thus, it may need to determine the effect of different doses of metformin on each component of MetS, which will be beneficial to early intervention and possible treatment of any related disease. The present study was designed to evaluate and compare the effect of different doses of metformin tablets monotherapy (500 mg/day and 1000 mg/day) on metabolic syndrome components, with focus on women with type 2 diabetes mellitus in Gorgan, South East of Caspian Sea.

MATERIALS AND METHODS

From 250 type 2 diabetic patients, forty women patients diagnosed with type 2 diabetes mellitus (T2DM) who were treated by metformin tablets monotherapy were invited to participate and forty age matched healthy women were included in this study. The samples were collected and carried out in the private laboratory in Gorgan, South East of Caspian Sea, Iran. Our study condition was different with other studies. The type 2 diabetic patients were new case and they received metformin tablets for 12 months. They used these two doses of metformin from the beginning of our study. The patients were chosen with causal method and if each patient had our study condition then we selected them for our study. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The written informed consent was taken from all patients and healthy controls. The type 2 diabetic patients received 500 mg/day (20 type 2 diabetic patients) and 1000 mg/day (20 type 2 diabetic patients) metformin tablets monotherapy for 12 months. Patients in type 2 diabetic patients were followed up and they were on a carbohydrate restricted diet and no exercise. The doses of metformin that we used for type 2 diabetic patients (500 mg/day and 1000 mg/day) for 12 months were different with other studies (especially the time condition, novelty of study). The healthy subjects were selected from among health care workers or from patient’s relatives. There were no metabolic syndrome, no drug consumption
and no some other diseases, etc. among healthy subjects. Patient’s medical records collected and controlled with the help of patient information. Patients with type 1 diabetes, renal failure, hepatobiliary disease and hypothyroidism were excluded from the study.

The US National Cholesterol Education Program Adult treatment Panel III criteria were utilized to determine metabolic syndrome components\(^\text{19}\). These criteria consist of:
1. Waist circumference $\geq 102$ cm (male), $\geq 88$ cm (female).
2. Triglyceride $\geq 150$ mg/dl, 
3. HDL-cholesterol $< 40$ mg/dl (male), $< 50$ mg/dl (female).
4. BP $\geq 110/\geq 85$ mmHg.
5. Fasting blood glucose $\geq 110$ mg/dl.

Metabolic syndrome was determined according to ATPIII criteria\(^\text{19}\), if the subjects have three or more above mentioned criteria.

Body mass index (BMI) was measured using the metric measuring scale and formula weight (kg)/height (meters)\(^2\). Waist circumference was measured using a tape in centimeters. Blood pressure was measured with a digital blood pressure monitor (Omron 70 JCP; Omron Matsusaka, Mie-Ken, Japan). Blood samples were provided for all subjects after 12 hrs fasting periods. All patients with type 2 diabetes mellitus had blood glucose higher than 126 mg/dL. Serum fasting blood sugar, total cholesterol, low-density lipoprotein (LDL)-cholesterol, high-density lipoprotein (HDL)-cholesterol, triglycerides and Hemoglobin A1C (HbA1C) measured by an automated enzymatic method. Insulin was determined by the ELISA commercial kit.

**Statistical analysis**

The SPSS Statistical Package was used to analyze the data (Version 16.0, Chicago, USA for Windows). The data were shown as mean ± SD and percentage. The Chi-square test was used to determine the prevalence of metabolic syndrome in two groups of patients. Independent paired samples t-test was used to compare data between metformin received and control groups. The correlation between variables was determined by Pearson’s correlation coefficient (r). P-Values lower than 0.05 were considered significant.

**RESULTS**

Table 1 shows the demographic and clinical characteristics of type 2 diabetic patients. A significant differences were found between the fasting blood sugar, triglycerides, high-density lipoprotein (HDL)-cholesterol, hemoglobin A1C (HbA1C) and insulin of the patients received 500 mg/day and 1000 mg/day metformin monotherapy ($p<0.001$).

| Parameters | Type 2 diabetic patients received 500 mg metformin (n=20) | Type 2 diabetic patients received 1000 mg metformin (n=20) | P-value |
|------------|----------------------------------------------------------|----------------------------------------------------------|---------|
| Mean age (years) | 43.28 ±28.45 | 42.62 ± 26.32 | 0.780 |
| Body Mass Index (BMI) | 24.29 ±12.08 | 23.43 ± 8.21 | 0.564 |
| Waist circumference (cm) | 88.72 ± 20.16 | 88.87 ± 22.12 | 0.878 |
| Systolic blood pressure (mmHg) | 135.46 ± 15.23 | 130.55 ± 18.34 | 0.234 |
| Diastolic blood pressure (mm Hg) | 83.12 ± 12.0 | 80.14 ± 8.70 | 0.279 |
| Fasting blood glucose (FBS) (mg/dL) | 99.76 ± 17.65 | 86.33 ± 18.58 | 0.001 |
| Fasting serum triglyceride(mg/dL) | 135.89 ± 36.78 | 120.75 ± 48.89 | 0.001 |
| Total cholesterol (mg/dL) | 211.62 ± 67.32 | 205.46 ± 56.92 | 0.923 |
| Fasting low density lipoprotein (LDL) cholesterol (mg/dL) | 132.56 ± 27.88 | 128.36 ± 32.36 | 0.832 |
| Fasting high density lipoprotein (HDL) cholesterol (mg/dL) | 58.85 ± 12.17 | 68.76 ± 14.21 | 0.001 |
| HbA1c level (%) | 6.80 ± 1.30 | 5.0 ± 1.50 | 0.001 |
| Insulin (µIU/mL) | 4.59 ± 5.25 | 8.78 ± 4.36 | 0.001 |
### Table 2: Demographic and clinical characteristics of type 2 diabetic patients received 500 mg metformin and controls

| Parameters                              | Type 2 diabetic patients received 500 mg metformin (n= 20) | Controls (n= 40) | P-value |
|-----------------------------------------|-----------------------------------------------------------|------------------|---------|
| Mean age (years)                        | 43.28 ± 28.45                                             | 42.67 ± 18.42    | 0.892   |
| Body Mass Index (BMI)                   | 24.29 ± 12.08                                             | 24.77 ± 8.92     | 0.776   |
| waist circumference (cm)                | 88.72 ± 20.16                                             | 88.36 ± 12.13    | 0.975   |
| Systolic blood pressure (mmHg)          | 135.46 ± 15.23                                            | 133.22 ± 15.21   | 0.332   |
| Diastolic blood pressure (mm Hg)        | 83.12 ± 12.0                                              | 81.15 ± 6.52     | 0.674   |
| Fasting blood glucose (FBS) (mg/dL)     | 99.76 ± 17.65                                             | 109.66 ± 12.25   | 0.001   |
| Fasting serum triglyceride (mg/dL)      | 135.89 ± 36.78                                            | 148.22 ± 25.14   | 0.001   |
| Total cholesterol (mg/dL)               | 211.62 ± 67.32                                            | 210.13 ± 48.16   | 0.989   |
| Fasting low density lipoprotein (LDL) cholesterol (mg/dL) | 132.56 ± 27.88                                           | 130.21 ± 18.12   | 0.967   |
| Fasting high density lipoprotein (HDL) cholesterol (mg/dL) | 58.85 ± 12.17                                             | 50.33 ± 8.19     | 0.001   |
| HbA1c level (%)                         | 6.80 ± 1.30                                               | 5.82 ± 1.70      | 0.001   |
| Insulin (µIU/mL)                        | 4.59±5.25                                                 | 18.22±2.60       | 0.001   |

The metabolic syndrome components (except waist circumference and blood pressure) and HbA1c levels in patients received 1000 mg/day metformin were lower and HDL-cholesterol and insulin levels were higher than those patients received 500 mg/day metformin. No significant differences were found between other parameters treated with metformin in both groups (p> 0.5) (Table 1).

Table 2 shows demographic and clinical characteristics of type 2 diabetic patients received 500 mg metformin and control groups. There were significant differences between the fasting blood sugar, triglycerides, high-density lipoprotein (HDL)-cholesterol, hemoglobin A1C and insulin of the patients received 1000 mg/day and control groups (p< 0.001).The fasting blood sugar, triglycerides, hemoglobin A1C and insulin were lower and high-density lipoprotein (HDL)-cholesterol was higher in patients received 1000 mg/day metformin than control groups (Table 3). No significant differences were found between other parameters treated with metformin in both groups (p> 0.5) (Table 3).

Correlations between variable pairs and different doses of metformin monotherapy are shown in Table 4. In both study groups a positive correlation was found between blood glucose and HbA1c and, blood glucose and triglyceride levels (p< 0.001), but the correlation in 1000 mg/day metformin therapy was stronger than 500 mg/day metformin therapy. There were a weak negative correlation between HbA1c and HDL-Cholesterol (p< 0.05) (Table 4). No significant differences were found between glucose-insulin and insulin-HDL-cholesterol.

The prevalence of metabolic syndrome in 500 mg/day and 1000 mg/day received type 2 diabetic patients were 15% and 10%, respectively (Not shown).
Table 3: Demographic and clinical characteristics of type 2 diabetic patients received 1000 mg metformin and controls

| Parameters                        | Type 2 diabetic patients received 1000 mg metformin (n= 20) | Controls (n= 40) | P-value |
|-----------------------------------|-------------------------------------------------------------|------------------|---------|
| Mean age (years)                  | 42.62 ± 26.32                                               | 42.67 ± 18.42    | 0.992   |
| Body Mass Index (BMI)             | 23.43 ± 8.21                                                | 24.77 ± 8.92     | 0.678   |
| waist circumference (cm)          | 88.87 ± 22.12                                               | 88.36 ± 12.13    | 0.978   |
| Systolic blood pressure (mmHg)    | 130.55 ± 18.34                                              | 133.22 ± 15.21   | 0.870   |
| Diastolic blood pressure (mm Hg)  | 80.14 ± 8.70                                                | 81.15 ± 6.52     | 0.773   |
| Fasting blood glucose (FBS) (mg/dL)| 86.33 ± 18.58                                               | 109.66 ± 12.25   | 0.001   |
| Fasting serum triglyceride(mg/dL) | 120.75 ± 48.89                                              | 148.22 ± 25.14   | 0.001   |
| Total cholesterol (mg/dL)         | 205.46 ± 56.92                                              | 210.13 ± 48.16   | 0.567   |
| Fasting low density lipoprotein (LDL) cholesterol (mg/dL) | 128.36 ± 32.36                                              | 130.21 ± 18.12   | 0.628   |
| Fasting high density lipoprotein (HDL) cholesterol (mg/dL) | 68.76 ± 14.21                                               | 50.33 ± 8.19     | 0.001   |
| HbA1c level (%)                   | 5. 0 ± 1.50                                                 | 5.82 ± 1.70      | 0.001   |
| Insulin (µIU/mL)                  | 8.78 ± 4.36                                                 | 18.22 ± 2.60     | 0.001   |

Table 4: Pearson’s correlation test applied to some metabolic syndrome components, HbA1c and insulin

| Variables                        | 500 mg/day metformin | 1000 mg/day metformin |
|-----------------------------------|----------------------|-----------------------|
|                                   | r        | P       | R       | p       |
| Glucose-HbA1c                     | 0.15     | < 0.05  | 0.29    | < 0.001 |
| Glucose- Triglycerides            | 0.12     | < 0.05  | 0.20    | < 0.001 |
| Glucose- Insulin                  | -0.07    | > 0.05  | -0.06   | > 0.05  |
| HbA1c- HDL-Cholesterol            | -0.62    | < 0.05  | -0.71   | < 0.05  |
| Insulin- HDL-Cholesterol          | 0.18     | > 0.05  | 0.15    | > 0.05  |

DISCUSSION

This study showed that treatment of type 2 diabetic patients with 1000 mg/day metformin monotherapy indicated significantly better effect on some metabolic syndrome components than those treated with 500 mg/day metformin. Patients with 1000 mg/day metformin therapy revealed lower fasting blood sugar, triglyceride and HbA1c and higher HDL-cholesterol and insulin than in patients treated with lower doses of metformin. The 1000 mg/day metformin treated patients produced a better effect than those treated with 500 mg/day metformin when compared with control groups. Our results show metformin monotherapy improved, especially fasting blood sugar, HDL-cholesterol, HbA1c and insulin levels. This may mean that 1000 mg/day metformin monotherapy has a more beneficial effect on these parameters and glycemic control, but not on blood pressure and all lipid profiles. Although the mechanism of metformin effect is not exactly clear. The most important variables for the evaluation of metabolic syndrome are triglyceride and HDL-cholesterol. Some study showed that the metformin produces a more favorable effect on metabolic syndrome components. Many studies...
assessed the metformin effect on lipid profile and blood pressure, while other findings showed an association of metformin with lipid profile in non-diabetic patients. Some studies reported a decrease of triglyceride, while other studies indicated a decrease of total cholesterol and triglycerides and an increase of HDL-cholesterol. Metformin in our study decreases triglyceride and increase HDL-cholesterol significantly in comparison with control groups. Some studies have indicated that metformin decreased blood pressure which is not in accordance with our study, while in agreement with our study; some others did not reveal any effect of metformin on blood pressure. Findings of Mourao Junior et al. showed that metformin received type 2 diabetic patients produced a significantly decreased WC, FBS, triglycerides and non-significant effects on blood pressure and on HDL-cholesterol. Some of these findings are in accordance (Fasting blood sugar, triglyceride) with our results and some others are not in agreement with our findings (HDL-cholesterol). Different studies demonstrate that metformin is effective in decreasing insulin resistance. Several studies indicated that metformin has an effect on total cholesterol (TC), triglycerides (TG), and HDL-cholesterol (HDL-C) levels, and on blood pressure and body mass index (BMI). The metformin did not significantly decrease blood pressure in our study agrees with other studies while other studies reported the decrease of systolic blood pressure and diastolic blood pressure with metformin. The different results are indicated about the effect of metformin on lipid profile. Some studies reported decrease in TC levels, while others showed reduction of TC and TG with an increase of HDL-C. Some other studies revealed no alterations in lipid profile. Some of these findings are partially in accordance with our study. Studies of Garber et al. indicated that the drug’s efficacy is dose-dependent. They reported that the minimal and maximal efficacious dose of metformin were 500 mg/day and 2000 mg/day, respectively. Some studies have shown that treatment with 500 mg/day metformin in type 2 diabetic patients decreased fasting plasma glucose and HbA1c, but the patients treated with 2000 mg/day showed the reduction of these parameters when compared with patients treated with 500 mg/day metformin therapy. These findings are almost similar to our study. Several studies have shown the beneficial effect of metformin in non-obese diabetic patients. It is reported that the decrease of HbA1c by metformin was not significantly different between non-obese and obese Japanese type 2 diabetic patients for 12 months metformin treatment. Studies showed a significant decrease in HbA1c levels in patients with a normal BMI when compared with obese type 2 diabetic patients for 12 months metformin treatment. It has also reported that metformin was more effective in type 2 diabetic patients with a lower BMI. These findings were in accordance with our results in patients received 1000 mg/day metformin monotherapy for 12 months. Different other studies indicated the metformin in non-obese and obese type 2 diabetic patients produce the similar glucose-lowering effect for study from 3 to 12 months. It is also reported that metformin was efficacious in non-obese type 2 diabetic patients. The glucose-lowering effect of 500 mg/day and 1000 mg/day metformin monotherapy on glucose, triglyceride and HbA1c and an increasing effect on HDL-cholesterol were seen in the present study and also the alteration of some metabolic syndrome components was achieved for one year treatment of non-obese type 2 diabetic patients with metformin. In the patients treated with 1000 mg/day metformin, HbA1c levels reached an ideal metabolic control (HbA1c: 5.0 ± 1.50%). It seems that the rate of decrease of HbA1c was faster in patients receiving high dose of metformin than low dose. Our results suggest that type 2 diabetic patients received 1000 mg/day metformin therapy required no addition of other treatments after the initiation of metformin. The patient may benefit the use of metformin monotherapy in the treatment of type 2 diabetic patients. By using different doses of metformin, our correlation study indicated that 1000 mg/day metformin therapy may show more effect on some metabolic syndrome components and HbA1c levels than those treated with 500 mg/day metformin in type diabetic patients. In our study, there was a strong positive association between fasting blood glucose and HbA1c and, fasting blood glucose and triglyceride in type 2 diabetic patients treated with 1000 mg/day metformin.
compared with those treated with 500 mg/day metformin, but there was a weak negative association between HbA1c and HDL-cholesterol in the both groups. It is reported there are a positive correlation between fasting blood glucose and HbA1c which is similar to the results of our study.

Different studies have shown the possible molecular mechanism of metformin action which are started by the drug’s activation of adenosine monophosphate (AMP)-activated protein kinase (AMPK). This enzyme causes suppression of glucose production via gluconeogenesis pathway and increased peripheral glucose uptake. Metformin inhibit the hepatic gluconeogenesis pathway by phosphorylation and activation of AMPK through AMPK-dependent regulation of the orphan nuclear receptor small heterodimer partner, SHP and a protein-threonine kinase (LKB1), which shows the lowering effect of metformin. The mechanism of metformin action on AMPK activity is not exactly cleared. Metformin is a drug that it may exert a direct effect on pancreatic β-cells. The effect of metformin on β-cell function is still unclear. Different studies also have revealed that in human, metformin may had effect on pancreatic β-cell function and increased insulin release in response to glucose. In vitro studies on rat islets cell indicated high levels of glucose and free fatty acids may have negative effect on metformin restored insulin secretion to β-cells. The molecular mechanisms of metformin effect on β-cell function remain unknown.

The most important part of our study design was one year metformin monotherapy, matched age between patients and control groups, and normal BMI of women type 2 diabetic patients and control groups. Several studies have shown the effects of gender on the MS in different populations. In American white and blacks, Mexican American, Korea, Iran, India, Oman, women had higher prevalence of metabolic syndrome than men. The study in Gorgan showed that females were more affected than males. Different studies have indicated that prevalence of metabolic syndrome increases with age. In our study, only women with closed average age were participated. Thus, the age and gender effects on metformin monotherapy, metabolic syndrome and their components were avoided in our study.

The results of this study had limitation. It is difficult to study the longtime treatment of metformin monotherapy of type 2 diabetic patients. The most referred type 2 diabetic patients did not have the conditions to participate in our study such as anti-diabetic combination drug therapy, duration of diabetes more than 1 year, gender (Only women type 2 diabetic patients) and age were limited our sample size.

CONCLUSION

In conclusion, our study showed the efficacy of the 1000 mg/day metformin monotherapy on better control of blood sugar, HbA1c, triglyceride and HDL-cholesterol levels, but Metformin had no effect on waist circumference and blood pressure. Treatment with this dose of metformin may be more beneficial for type 2 diabetic patients than those other doses.

Declarations:

Ethics approval and consent to participate: The ethnic committee of Golestan University of Medical Sciences approval the study (With ethics number: IR.GOUMS.REC.1399.273).

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تأثير الجرعات المختلفة من أقراص الميتروفورمين على مكونات متلازمة التمثيل الغذائي لدى النساء المصابات بداء السكري من النوع 2 في جرمان (جنوب شرق بحر قزوين) من ميرزاى - نجف، منصور اميرای - ماجد مرجاني 

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أظهرت بعض الدراسات التي أجريت على الأدوية المضادة لفرط سكر الدم عن طريق الفم أنها تساعد وتواصل مرضا السكري من النوع الثاني. سمحت الدراسة الحالية لتقييم ومقارنة تأثير الجرعات المختلفة من أقراص الميتروفورمين على مكونات متلازمة التمثيل الغذائي لدى النساء المصابات بداء السكري من النوع 2 في جرمان، جنوب شرق بحر قزوين. تلقت أربعون مريضة من مرضا السكري من النوع الثاني 500 مجم يوم و1000 مجم يوم من أقراص الميتروفورمين لمدة 12 شهرا، وتم تضمن أربعين من السيدات الأخصائية في هذه الدراسة. استخدمت معايير ATP III لتحديد مكونات متلازمة التمثيل الغذائي، وتم قياس ملامح الدهون، والأنسولين. وجدت فروق ذات دلالة إحصائية بين HbA1c، والأنسولين في الدراسية الذين تلقوا 500 مجم يوم و1000 مجم يوم من الميتروفورمين كعلاج وحيد. كانت نسبة السكر في الدم والدهون الثلاثية والأنسولين أقل بكثير في المرضى الذين تلقوا 1000 مجم يوم من الميتروفورمين بالمقارنة بالمجموعه الضابطة. في كلما المجموعتين، كان الكولسترول أعلى من المجموعات الضابطة، لكن في HbA1c كان الكولسترول أقل من المجموعات الضابطة، ولكن في HDL المرضى الذين تلقوا 500 و 1000 مجم يوم من الميتروفورمين، أظهرت دراستنا فعالية 1000 مجم يوم من العلاج بالبيكلورمين الأحادي في التحكم بشكل أفضل في نسبة السكر في الدم، والدهون الثلاثية، والكولسترول الحمضي. ولكن لم يكن للميتروفورمين أي تأثير على محتوى الخصر وضغط الدم. قد يكون العلاج بهذه الجرعة من الميتروفورمين أكثر فائدة لمرضى السكري من النوع 2 من تلك الجرعات الأخرى.

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