ISSN 1991- 8690 الترقيم الدولي 1991 - 8690

Effects of Metformin and diet on hemoglobin, cholesterol and triglyceride levels of Type 2 diabetic Patients

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Summary:

Metformin is recommend as the first line oral agent to be used patients with non-insulin-dependent diabetes mellitus(Type 2 Diabetic).The study was prospectively performed in diabetic and endocrine center of Nassiriyah city .The present study aimed to shed light on metformin and hemoglobin(Hb) and lipid profile in type II diabetic patients with diet and without diet . Our study included 60 patients treated with metformin for Twelve-week . The subjects were divided into three groups. Group I as control, group II patients received Metformin- (1000/2 mg/day) with diet and group III patients received the Metformin-(1000/2 mg/day) without diet all these patient had been selected from those patients visit . The Hb concentration and lipid profile were been examine after 3 months of treatment.In present study we found the hemoglobin concentration reduced in group II with diet patient compare with the group III and control group also reduced in the group III without diet patient compare with control group, as same time This study showed that the treatment with metformine led to, reductions observed in the cholesterol concentrations of the group II diabetic patients with diet compared with the group III administered MET respective without diet diabetic and compared with control, Also we found the triglyceride concentrations of diabetic patients in group administered MET respective with diet were significantly ($p<0.05$) reduced compared with that of without diet diabetic and control therefore it was considered predisposing factor to reduced damage diabetes. For this reason; continuous taking of metaformin should be important in medicine and general healthy, and they must be not used unless consult of specialists.

Keywords: Metformin, type II diabetes, lipid profile, hemoglobin

Introduction:

Metformin (dimethylbiguanide) is an orally administered drug used for lowering blood glucose concentrations in patients with non-insulin-dependent diabetes mellitus (Buse *et al.,* 2016). Metformin is a medicine in a class called biguanides, is decreasing the amount of glucose released into the bloodstream by the liver and act as an "insulin sensitizer," that lead to lowers blood sugar levels (Kim *et al.,*2014).The drug is absorbed well from the intestine. Nor combine medication with blood proteins and is not metabolized in the liver and is ejected in a non-volatile in the urine .The half-life of the drug ranges between 1.5-3 hours (Gong *et al., 2012*).Young *et al.,* (2008) recorded metformin was also effective in type 1 diabetic patients of normal body weight with insulin therapy. According to (Graham*et al.,* 2011) they have made clear that the mechanical action of metformin is its propensity to reduce hepatic gluconeogenesis ,glucose output ,improve peripheral glucose outtake and utilization in insulin-sensitive tissues like adipose tissues and muscles and Perhaps the drug works on the intestine, where reduces the transmission of glucose.

Mechanical work property specifically is unclear but there is a reference to the one that works by activating of an intercellular AMP-activated protein kinase, (Shaw *et al* .,2005). There are other uses for metformin is prescribed for patients with polycystic

ovary syndrome (PCOS) (Pasquali *et al* .,2000). Kim *et a.,l* (2014) had recorded Metformin inhibited the inflammatory response in a rheumatoid arthritis mouse model. In another study conducted by koh *et al.,* (2014) , where they noticed Metformin has also been demonstrated to have an anti-inflammatory activity in an inflammation-associated tumor mouse model .In clinical studies, metformin, alone or in combination with a sulfonylurea, lowered triglycerides, total cholesterol, and LDL cholesterol levels and had no adverse effects on other lipid levels. Metformin is associated with improvements in lipoprotein metabolism (Glueck *et al.,* 2001) Featuring metformin for drugs sulfonylureas and insulin thus no effect on the beta cells in the pancreas where the work mechanism does not rely on the secretion of insulin from the pancreas, and as a result, the drug metformin does not cause a rise in the level of insulin in the blood and therefore dysfunctional to a sharp drop in blood sugar when used alone, as happens with sulfonylurea drugs or insulin.These drugs do not cause weight gain in patients, as observed when using a sulfonylurea medicines or insulin. This may be due to metformin does not alert the appetite to eat when the patient. Thus, the drug metformin is considered one of the best medicines for patients obese people with type II diabetes (Bolen *et al.,* 2007, Roumie *et al.,* 2010).The non-insulin-dependent diabetes mellitus (Type II diabetes mellitus) is a a metabolic disease associated with beta cells of pancreas dysfunction or insulin action on target cells (Hossain *et al.,* 2012) . Type 2 diabetes mellitus is a global health problem and one of the major causes of morbidity and mortality, characterized by hyperglycaemia and disturbance of glucose metabolism. The incidence of the disease is high worldwide and varies between populations because of differences in genetic susceptibility and other modifiable risk factors. Quaseem *et al* .,2007

Material and methods

Samples of study

The study was conducted by collecting blood samples from 60 people (23males and 37females) the average age of between 35-60 years old which have be suffering from diabetes type II and administer metformin as a regulator of the level of glucose in the blood and they attending regularly to diabetic and endocrine center of Nassiriyah city after recorded case history for each patient , samples of patients divided to two groups : diabetic Type II group used metformin with diet(group II) and a diabetic type II and also used metformin but without diet (group III). In addition to assembling control samples (group I) from 20 voluntarily' healthy pupils for the purpose of comparison between groups.

Biochemical analysis

About 5 ml of plain venous blood sample was obtained by venepuncture from patients and controls after obtaining informed consent form , Use 1 ml of whole blood to measure hemoglobin concentration and the remainder of the blood sample separated by centrifuge to obtain serum which use to determination lipid profile(cholesterol and triglyceride)

Statistical Analysis:

Standard analysis of the data of different studied group was performed using the computerized statistical program: The SPSS program (Statistical Program for Social Sciences). The results were expressed as mean± standard Error (x± S.E). Analysis of variance (ANOVA) was used to compare the results of different groups. The differences are considered to be significant at ($P \leq 0.05$).

Results

Effects of metformin, on Hb concentration

For the results of the concentration of hemoglobin in the blood, there was a significant decrease ($p<0.05$) in the level of hemoglobin in group II and group III compared with the control group, at the same time it was noted that there was a significant decrease in the concentration of hemoglobin in the group II compared to the group III (table 1).

(Table 1) Effect of metformen on hemoglobin to patient with diet and without diet

Groups	Hb g/dl
Control group	14.38 ± 0.15^{a}
GroupII	11.94 ± 0.21^{b}
Group III	13.10 ± 0.29^{c}
LSD	1.15

Values are means ± S.E.

Different letters refer to significant differences ($p<0.05$).

Same letters refer to no significant differences ($p<0.05$).

Effects of metformin, on serum cholesterol concentration:

Analysis of data showed there was a significant increase ($p<0.05$) in the cholesterol level in group II and group III compare with the control group, also there was a significant increase in the cholesterol level in group III ,where (table 2).

(Table 2)Effect of metformen on cholesterol of patient with diet and without diet

Groups	Cholesterol mg/dl
Control group	94.60±3.16 ^{c}
Group II	177.26±6.95^{b}
Group III	186.47±7.77^{a}
LSD	9.21

Values are means ± S.E.
Different letters refer to significant differences ($p<0.05$).
Same letters refer to no significant differences ($p<0.05$).

Effects of metformen on serum triglyceride level:

Results of statistical analysis showed there was a significant increase ($p<0.05$) in the level of triglyceride in group II and group III compared with the control group ,also there was a significant difference between group II and group III, where there was a decrease in level of triglyceride in the group II When compared with group III (Table 3).

(Table 3)Effect of metformen on triglyceride to patient with diet and without diet

Groups	Triglyceride mg/dl
Control group	100.34±2.91^{c}
Group II	162.52±1.54 ^{b}
Group III	231.52 ±3.04 ^{a}
LSD	6.96

Values are means ± S.E.
Different letters refer to significant differences ($p<0.05$).
Same letters refer to no significant differences ($p<0.05$).

Discussion:

Diabetes type II is the most prevalent form and more commonly associated with insulin resistance in the presence of an associated impairment in compensatory insulin secretion and associated with obesity, (Yousif ,2011). Previous studies concentrated on the relationship of oral hypoglycemic agents like metformin and diet their importance in diabetic patients , Ajagbonna *et al.*, 1999) observed that administration. of medicinal compounds or drugs can alter the normal range of hematological parameters this is because it plays a role in physiological, nutritional and pathological state of an organism. Diabetes mellitus is known to cause anemia of chronic disease, erythrocyte, leukocyte and platelet dysfunction(Gkrania *et al* 2010) Waggiallah and Alzohairy (2011) has observed anemia is increased in patients with diabetes. As result of multifactorial. Chronic hyperglycemia causes abnormal red blood cells and renal sympathetic denervation is associated with autonomic neuropathy and oxidative stress . decreased in amount of erythropoietin produced by the peritubular fibroblasts due to Hypoxic environment which occurs in the renal tubule interstitial.the most important reason of anemia in diabetic patients (Bosman *et al*., 2001).In diabetes, reduced haemoglobin has been reported (Mansi, 2006). Reduction in haemoglobin may be accompanied by a fall in the red blood cell count and packed cell volume (Muhammad and Oloyede, 2009).Very low readings of RBC haemoglobin and hematocrit could indicate anaemia (Muhammad and Oloyede, 2009). so there are a number of studies are consistent with our study which indicating that metformin causes a decrease in the level of hemoglobin .

In the present study, serum cholesterol and triglyceride were measured in diabetic patients. There is significant reduction in serum cholesterol and triglyceride in diabetic patients as compare with normal healthy subjects. Interestingly, similar observation has been reported with diabetic rats treated with Metformin respectively in previous study(Chehade and Mooradian, 2000*;* Zannah *et al.*, 2014). This could be due to increased breakdown of the cholesterol in the liver, and decreased absorption of cholesterol via the chylomicrons due to inhibition of α-glucosidase enzymes. The above result suggests that the administration of Metformin, may improve lipid dysfunction and hence retard the development of diabetic complications. This could be attributed to their promotion of utilization of glucose and hence depressed mobilization of fats.

It is well known that in uncontrolled diabetes mellitus, there will be an increase in total cholesterol, triglyceride with a concomitant decrease in the HDL-C which contributes to coronary artery disease (Arvind *et al*., 2002*;* Selvan *et al.,* 2008). This could be attributed to abnormalities in lipid metabolism due to diabetes-induced hyper triglyceridaemia and hypercholesterolaemia (Mitra *et al.,* 1995). The increase in blood cholesterol and triacylglycerol concentrations may be due to the action of hormone sensitive lipase, which promotes lipolysis and subsequently increases the level of free fatty-acids and triacylglycerol in circulation. The free fatty acids are catabolized to acetyl-CoA which is further channeled to cholesterol synthesis; thus, increasing blood cholesterol level (Oyedepo, 2012). Zainab *et al*.,(2016) suggested that Metformin alone produce a non-significant favorable effect on all lipids profile parameters, while metformin furthermore glibenclamide appeared a significant reduction in Triyglycerid.

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