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Original Article

Outcomes of Metformin on Lipid Profile of Type II Diabetes Mellitus Cases in Tertiary Care Hospital

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ABSTRACT

Background: *Metformin acts mainly at the liver by reducing glucose output and secondarily, by augmenting glucose uptake in the peripheral tissues, primarily muscle. These effects are facilitated by the activation of an upstream kinase, liver kinase B1 (LKB-1), which in turn controls the downstream kinase adenosine monophosphates protein kinase (AMPK). AMPK phosphorylates a transcriptional co-activator, transducer of regulated CREB protein 2, resulting in its inactivation which consequently down regulates transcriptional events that promote synthesis of gluconeogenic enzymes.*
Methods: *200 total numbers of cases were included of diabetic mellitus who received 1500mg/day metformin. The duration of study was one year.*
Results: *It is observed that there is decrease in fasting blood glucose, total cholesterol, LDL- C and TGs. HDL-C levels were increased significantly after treatment.*
Conclusions*: Therefore, the findings of the present study concluded that metformin used in diabetic treatment improves lipid profile.*

Keywords: *Metformin, Gluconeogenesis, Diabetes Mellitus*

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INTRODUCTION

In cardiovascular disease (CVD), dyslipidemia is one of the major one. It plays an important role in the progression of atherosclerosis, the underlying pathology of CVD. Dyslipidemia is very much prevalent in type 2 diabetes with respect to the general population.[1] It is caused by the interrelation among obesity, insulin resistance and hyperinsulinism.[2] In one of their study Freedman et al (1999) compared overweight subjects with their respective thinner counterparts, they found 2.4 to 7.1 times higher probability to have an elevated total cholesterol, LDL cholesterol, triglycerides and blood pressure as well as 12.6 times higher probability to have hyperinsulinemia in overweight subjects.[3] Results suggest that the fatty tissue is solely related to risk factors, such as insulin resistance syndrome, which can lead to cardiovascular complications.[4] It is most commonly characterized by elevated TG and reduced HDL-C in type 2 diabetic patients.[5] These abnormalities can be present alone or in combination with other metabolic disorders. According to Wood et al, 1972; Berrios et al, 1997, the prevalence of dyslipidemia varies depending on the population studied, geographic location, and socioeconomic development etc. The discovery of metformin began with the synthesis of galegine-like compounds. It is derived from Gallega officinalis, a plant traditionally employed in Europe as a drug for diabetes treatment for centuries.[6] Metformin acts mainly at the liver by reducing glucose output and secondarily, by augmenting glucose uptake in the peripheral tissues, primarily muscle. These effects are facilitated by the activation of an upstream kinase, liver kinase B1 (LKB-1),

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which in turn controls the downstream kinase adenosine monophosphatase protein kinase (AMPK). AMPK phosphorylates a transcriptional co-activator, transducer of regulated CREB protein 2, resulting in its inactivation which consequently downregulates transcriptional events that promote synthesis of gluconeogenic enzymes.[7] Inhibition of mitochondrial respiration has also been proposed to contribute to the reduction of gluconeogenesis since it reduces the energy supply required for this process.[8] When treating patients with type 2 diabetes mellitus, metformin's effectiveness, benefic cardiovascular and metabolic effects, and its capacity to be related with other antidiabetic agents makes this drug the first glucose lowering agent of choice. Developing countries are expected to shoulder the majority of the burden of diabetes.[9] The present study is concentrated on effect of metformin on lipid profile of type II diabetes patients.

METHODS

STUDY POPULATION: 200 total numbers of cases were included of diabetic mellitus who received 1500mg/day metformin.

STUDY DURATION: The duration of study was one year.

STUDY AREA: This study was conducted in the Department of Biochemistry & Pharmacology in the Patna Medical College, Patna, Bihar.

DATA COLLECTION: All subjects were selected from type II diabetes patients who are on treatment of only metformin (1500mg/daily). The parameters were performed after 3 months of treatment. FBS, TC, TGs, HDL-C, LDL-C and VLDL –C were measured. Initially the patients were selected without any treatment and found diabetes, later we started treating them with metformin (1500mg/daily). After three months of their treatment we measured all above mentioned parameters and compared with initial values. The ANOVA performed with t–test. The values expressed with mean and SD.

DATA ANALYSIS: Data were analyzed by using Statistic & Microsoft excel.

RESULTS

200 subjects were selected from diabetes type II patients who are on treatment of only metformin (1500mg/daily). The parameters were performed after 3 months of treatment. FBS, TC, TGs, HDL-C, LDL-C and VLDL –C were measured. This study showed 37% male & 63% female. In the present study found that,41.5% cases were belonging to 51-60 age group followed by 41-50 (30.5%) & 61-70(28%). Effect of metformin on 0 day,45,90 days of treatment which showed in table 3. In results it is observed that there is decrease in fasting blood glucose, total cholesterol, LDL- C and TGs. HDL-C levels were increased significantly after treatment.

Table 1: Distribution Of Cases According To Gender

GENDER	No. OF CASES	PERCENTAGE
MALE	74	37%
FEMALE	126	63%
TOTAL	200	100%

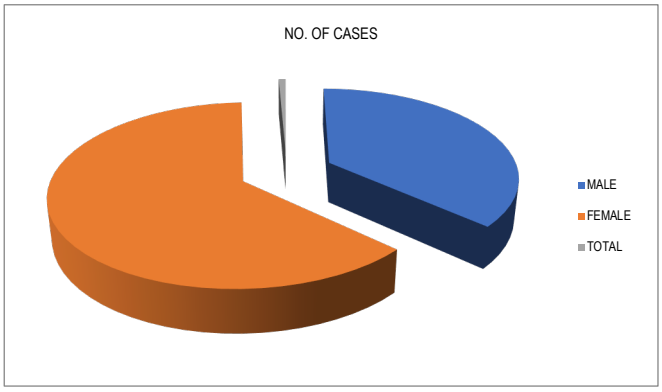

Chart: -1 This Chart Showing Distribution According To Gender

Table 2: Distribution Of Cases According To Age

AGE	No. OF CASES	PERCENTAGE
41-50	61	30.5%
51-60	83	41.5%
61-70	56	28%
TOTAL	200	100%

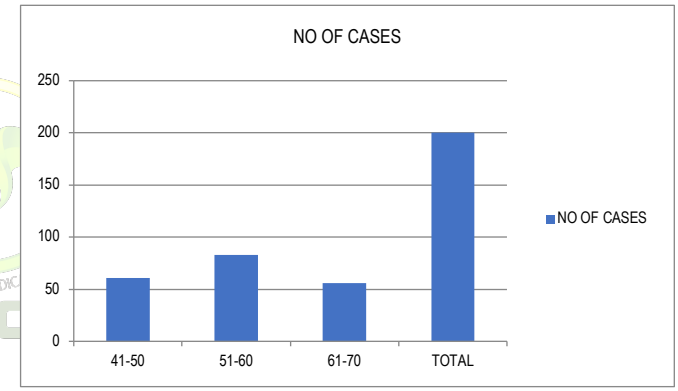

Chart: -2 This Chart Showing Distribution According To Age

Table 3: This Chart Showing Parameters

Parameters	0 day treatment	45 day treatment	90 day treatment	P value
FBS(mg/dl)	182.45±15.64	137.62±18.72	112.64±20.39	0.0009
TC(mg/dl)	209.72±30.76	192.64±21.65	165.72±7.65	0.0001
HDL-C(mg/dl)	24.11±4.56	29.57±7.60	32.76±8.92	0.0001
LDL-C(mg/dl)	147.34±20.28	130.15±6.43	105.42±3.51	0.0001
TGs(mg/dl)	188.92±24.93	161.73±15.47	148.61±5.74	0.0001

DISCUSSION

The results of the present study revealed the beneficial effect clearly after the 45th day of treatment in 90 days of treatment. It has been found that the use of metformin treatment in diabetic patient, corrected the dyslipidemia. In 6-week duration, a meta-analysis of 41 randomized, controlled assessments of metformin showed significant reductions in total cholesterol, LDL cholesterol and triglycerides in patients. It has been also observed in some nonrandomized studies that there are significant reductions in free fatty acids following treatment with metformin.[10] The metformin effect on lipid profile was modest and generally smaller than the effect

of the intensive lifestyle intervention in nondiabetic and with impaired glucose tolerance persons in the Diabetes Prevention Program.[11] UK Prospective Diabetes study suggests that reductions in the risk of macro vascular endpoints with metformin are associated with other mechanisms, not only the effects on lipids.[12] Metformin also declines oxidative stress, inhibits lipid peroxidation of LDL and HDL, and the production of the superoxide free radical in platelets. Metformin also decrease the production of advanced glycation end products indirectly, by reduction of hyperglycemia, and directly by an insulin independent mechanism.[13] Experimental studies observed that metformin may prevent the binding of monocytes to cultured vascular cells and differentiation of monocytes into macrophages and their transformation into foam cells.[14] In several studies, when compared with pre-treatment, a significant improvement in glycemic parameters (FBG) was found over a short period of 8-12 weeks in moderately severe, newly diagnosed diabetic patients treated with either glimepiride, metformin or combination.[15-17] The improvements in glycaemic parameters with glimepiride and metformin were similar, while combination produced a lower degree of reduction with respect to the change in FBG.[18-20] Previously it was found that in many studies that glimepiride increases insulin sensitivity at peripheral target sites and improve glycemic control in newly diagnosed diabetic subjects. The extra pancreatic effects of glimepiride with metformin made it more effective in improving glycemic control by decreasing glucose level.[21-22] Newly diagnosed type 2 diabetic patients show varying features with respect to lipid profile. The results of the present study are supported by the previous studies which demonstrated that metformin as monotherapy decreased TC, LDL-C, and TG levels[23-25] and increase serum HDL-C level.

CONCLUSION

Therefore, the findings of the present study concluded that metformin used in diabetic treatment improves lipid profile.

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