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A CROSS SECTIONAL STUDY IN NORTH EASTERN UTTAR PRADESH POPULATION FOR THE ESTIMATION OF BMI, HDL & TRIGLYCERIDES LEVELS IN RECENTLY DIAGNOSED PATIENTS WITH TYPE 2 DIABETES MELLITUS TAKING METFORMIN ALONE, METFORMIN WITH ADD ON SITAGLIPTIN AND SITAGLIPTIN ALONE.

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ABSTRACT

Objectives: To evaluate the role of Metformin, Sitagliptin & combination of both drugs in Body weight, HDL-C & Triglyceride levels in recently diagnosed patients of type 2 Diabetes mellitus. **Methods:** This cross-sectional study includes analysis of total 75 patients divided in 3 groups. Metformin group (2000 mgs), Sitagliptin group (100 mgs), Combination of both Metformin & Sitagliptin group (Metformin 1000 mg+ Sitagliptin 50 mg). Their body weight (BMI) & Laboratory investigations regarding HDL & Triglycerides were carried out and findings were noted in each follow-ups. **Results:** After 24 week onwards there were statistically significant reduction in BMI in each group but the in 3rd group (Combination group) the reduction in BMI was Most highly significant ($p<0.001$). On other hand HDL level was raised significantly ($p<0.01$) in all the three groups but in the Sitagliptin and combined group it was

most highly significant ($p<0.001$) observed from 24 week onwards, whereas in Triglyceride levels, Metformin and Sitagliptin, both group of patients showed significant ($p<0.01$) reduction. Metformin group showed significant ($p<0.01$) reduction earlier at 12 week and Sitagliptin showed significant reduction ($p<0.01$) later at 36 week. In the combined group it was insignificantly ($p>0.05$) fluctuating. **Conclusions:** In conclusion, significant differences was found in effects of Sitagliptin treatment on body weight (BMI) & HDL, Triglycerides level in patients recently diagnosed with type 2 Diabetes mellitus.

KEYWORDS: Type 2 diabetes mellitus, Body weight, HDL-C, Triglycerides, Metformin, Sitagliptin.

INTRODUCTION

Diabetes mellitus (DM), a widespread endocrine metabolic disorder, is an important cause of morbidity and mortality worldwide. Development of diabetes includes several pathogenic processes ranging from autoimmune destruction of the β-cells of the pancreas with consequent insulin deficiency to abnormalities that causes resistance to insulin action.[1]

Diabetic dyslipidemia is commonly diagnosed in diabetes mellitus, which is characterized by increased plasma levels of triglycerides, low-density lipoprotein cholesterol (LDL-C) and decreased levels of high-density lipoprotein cholesterol (HDL-C). Diabetic dyslipidemia complicates the management of diabetes mellitus and its complications such as cardiovascular, renal disorders, etc.[1]

The aim of this study is to assess efficacy of Metformin, Sitagliptin & combination of both on body weight & lipid profile.

MATERIALS AND METHODS

Totally 120 subjects were studied & all investigations were carried out. Out of these subjects, 75 subjects were coming regularly in all follow-ups. i.e. 3 months, 12 months, 24 months, 36 months. They were divided into three groups - 25 patients were in Metformin (group I), 25 patients were in Sitagliptin (group II) & 25 patients were in combination group (Metformin & Sitagliptin).

The random venous blood sample was taken and analyzed for lipid profiles in total 75 subjects within three groups.

Statistical analysis

Z test is used for statistical analysis. Various values of p were obtained. If $p>0.05$ was considered insignificant, whereas $p<0.05$ was less significant, $p<0.01$ was highly significant and $p<0.001$ was considered most highly significant. Statistical comparison was done between I, II and III groups.

RESULTS

The results showed the efficacy of the administered medications. Which demonstrates statistically significant reduction in BMI in each group after 24 week (3^{rd} visit) onwards, but the in 3^{rd} group patients taking combination of Metformin & Sitagliptin the reduction in BMI was Most highly significant ($p<0.001$). The fact behind reduction in BMI at 24 weeks (6 months) onwards suggests the duration of weight loss in subjects of the groups after beginning of the medications.

(TABLE 1)

HDL-C level was raised significantly ($p<0.01$) in all the three groups but in the Sitagliptin and combined group it was most highly significant ($p<0.001$) observed from 24 week onwards. (TABLE 2).

In Triglyceride level, Metformin and Sitagliptin, both group of patients showed significant ($p<0.01$) reduction. Metformin group showed significant ($p<0.01$) reduction earlier at 12 week and Sitagliptin showed significant ($p<0.01$) reduction later at 36 week. In the combined group it was insignificantly ($p>0.05$) fluctuating. (TABLE 3).

Table 1 shows Mean± S.D. of BMI of the three groups

Drug	Duration			
	0-Week	12-Week	24-Week	36-Week
Metformin	26.7±2.53	26.2±2.46	25.42±1.99	25.26±2.29
p		p>0.05	p <0.05	p <0.05
Sitagliptin	26.14±2.92	25.5±2.53	24.54±2.34	23.58±2.74
p		p>0.05	p<0.05	p <0.05
Metformin + Sitagliptin	26.54±2.05	25.58±1.99	24.62±1.79	23.98±1.29
p		p>0.05	p<0.01	p<0.001

Table 2 shows Mean± S.D. of HDL of the three groups

Drug	Duration			
	0-Week	12-Week	24-Week	36-Week
Metformin	34.76±4.26	39.24±4.81	39.2±4.12	40.8±4.49
p		p<0.01	p<0.01	p<0.001
Sitagliptin	33.16±3.99	36.68±4.22	38.6±3.92	39.24±4.25
p		p<0.01	p<0.001	p<0.001
Metformin + Sitagliptin	33.8±5.05	36.04±6.12	39.56±4.36	40.84±5.12
p		p>0.05	p<0.001	p<0.001

Table 3 shows Mean± S.D. of Triglyceride of the three groups

Drug	Duration			
	0-Week	12-Week	24-Week	36-Week
Metformin	194.6±48.78	188.36±50.35	180.04±39.25	171.72±35.66
p		p<0.05	p<0.05	p<0.05
Sitagliptin	171.72±28.97	161.32 ±24.07	161.32 ±19.06	156.48±24.98
p		p>0.05	p>0.05	p<0.05
Metformin + Sitagliptin	205.0±46.51	205.3±61.43	232.34±59.72	219.56±54.08
p		p>0.05	p>0.05	p>0.05

DISCUSSION

This study entitled "A cross sectional study in North Eastern Uttar Pradesh population for the estimation of HDL, Triglycerides levels in recently diagnosed patients with Diabetes Mellitus Type 2 taking Metformin alone, Metformin with add on Sitagliptin and Sitagliptin alone" is a comparative study performed in recently diagnosed patients of type 2 Diabetes mellitus. It was conducted in total 75 patients to establish the role of Metformin, Siatgliptin & Combination in reduction in Body weight & improvement in Lipid profile. i.e. HDL-C & Triglyceride levels.

The patients had been divided randomly into three groups of 25 patients in each group. Patients were recalled in 3 follow-ups. i.e. 12 weeks, 24 weeks, 36 weeks. After their 1st visit, along with calculation of BMI & their blood investigations such as serum HDL & Serum Triglycerides level were carried out & findings were noted in specially prepared case history proforma.

Result of our study is comparable to the studies conducted by Katsuyama et al.[2] who had observed that Body weight and BMI in obese group were significantly greater than in non-

obese group at baseline. After 6 months of initiating Sitagliptin use, significant reduction in body weight in obese group, whereas no change was noted in non-obese group, whereas Yanai et al.[3] had found a significant and negative correlation between change in body weight and body mass index at baseline. After 6 months they found a significant reduction in body weight. ($p<0.01$).

Another study performed by Seck et al.[4] result was for the PP cohort, Relative to baseline, Sitagliptin was associated with significant weight loss ($p<0.05$) (-1.6 kg) compared with weight gain (+0.7 kg) with glipizide. Study conducted by Yang et al.[5] in 2012 revealed a small decrease from baseline body weight in the placebo group compared with no change in the Sitagliptin group (between-group difference 0.5kg; $p<0.01$).

Lim S et al.[6] had also established that after 52 weeks, multivariate regression analysis indicated that the reduction in HbA1c was significantly associated with body mass index & other parameters. One more study conducted by Amjad et al.[7] which reveals significant difference in weight as well as other parameters for glycemic control in both groups Sitagliptin+ Metformin & Glimiperide group. In glimepiride group there was slight increase in weight (-2.7±2.23kg vs. +2.45±0.55kg, $p<0.01$). It was concluded that Sitagliptin, a DDP-4 antagonist is as efficacious as glimepiride in reducing HbA1C and fasting blood sugar. It also causes reduction in weight and is well tolerated.

Another study conducted by Demir S. et al.[8] had concluded that patients having inadequate glycemic control, the addition of a DPP-4 inhibitor as a second oral agent to Metformin monotherapy provides better glycemic control and does not cause weight gain. These effects depend on baseline C-peptide levels. Weinstain et al.[9] had observed that Sitagliptin/Metformin led to weight loss (-1.4 kg), while pioglitazone led to weight gain (3.0 kg) ($p<0.001$) for the between-group difference).

In contrast to these studies, a study performed by Shigematsu E. el al.[10] & Khalil et al.[11] had revealed that change in body weight and thus BMI was not significant. ($p>0.05$).

Other comparative studies reveal comparison of Lipid profiles include a study performed by Chawla S. et al.[12] revealed a significant ($p<0.01$) decrease in High density lipoprotein (HDL‑C) & a significant ($p<0.01$) decrease in Triglyceride, whereas Katsuyama et al.[2] had also established that significant differences was seen in effects of Sitagliptin treatment on

body weight and lipid metabolism between obese and non-obese patients with type 2 diabetes.

Another study performed by Sakamoto Y. et al.[13] had demonstrated that serum levels of triglycerides and total cholesterol decreased significantly. ($p<0.001$).

Pavithra N. et al.[1] had also demonstrated that the addition of glimepiride to Metformin in type 2 diabetes have beneficial effects on lipid profiles in addition to improved glycemic control throughout the study period.

Results are dissimilar to the present study & other studies include study conducted by Shigematsu E. el al.[10] had revealed changes of the lipid profile after Sitagliptin treatment, the HDL level & Triglyceride level were not significantly ($p>0.05$) reduced after 12 weeks of Sitagliptin treatment from baseline.

Garimella S. et al.[14] had revealed significant ($p<0.05$) reduction in triglycerides. The results were clearly indicated that beneficial effect of Metformin on lipid profile of type II diabetes. Hence concluded that Metformin having the ability to correct dyslipidemia in type II diabetic patients.

Fan M et.al.[15] had concluded that Sitagliptin alone or in combination significantly ($p<0.001$) improved serum HDL-C levels & serum triglycerides (TGs) in patients with type 2 diabetes mellitus.

Katsuyama et al.[2] had seen significant ($p<0.01$) and inverse correlation between change in TG and BMI at baseline. After 6 months, Serum TG was found significantly decreased while serum TG significantly increased. Sitagliptin reduced serum TG in a baseline- BMI-dependent manner.

Pavithra N.et al.[1] had assessed the lipid lowering effect of antidiabetic drugs such as Metformin & combination of Metformin & Glimepiride in type 2 diabetes mellitus patients. The results showed the efficacy of the administration of combination of Metformin and glimepiride simultaneously and Metformin as monotherapy. There were significant changes in triglycerides during the study period. The results of the present study have demonstrated that the addition of glimepiride to Metformin in type 2 diabetes have beneficial effects on lipid profiles in addition to improved glycemic control throughout the study period.

Mervat M. et al.[16] had demonstrated the effect of Sitagliptin monotherapy on lipid profile. Result revealed that Sitagliptin significantly ($p<0.01$) reduced TG. It was established that Sitagliptin monotherapy is effective in dyslipidemia in newly diagnosed T2DM.

CONCLUSION

- In Metformin group for testing significance of differences, Z test was applied. It was insignificant ($p>0.05$) at 12 weeks and but significant during 24 weeks and 36 weeks ($p<0.05$) indicating the fact that there was significant effect of the medication in reducing BMI. i.e. weight.
- In Sitagliptin group Z test was insignificant ($p>0.05$) at 12 weeks but significant differences were obtained during 24 weeks ($p<0.05$) and highly significant at 36 weeks ($p<0.01$), indicating the fact that there was significant effect of Sitagliptin on BMI after 24 weeks of initiating medication.
- In Combined group Z test was insignificant ($p>0.05$) at 12 weeks and highly significant ($p<0.01$) reduction obtained during 24 weeks and Most Highly Significant ($p<0.001$) at 36 weeks indicating the fact that there was highly significant effect of the Metformin + Sitagliptin medication on reduction of BMI after 24 weeks.

For HDL level

- In Metformin group, Z test applied was highly significant ($p>0.01$) at 12 weeks & 24 weeks and Most Highly significant ($p<0.001$) at 36 weeks, indicating the fact that there significant rise in HDL was seen after 12 weeks of initiating medication.
- In Sitagliptin group, Z test applied was highly significant ($p<0.01$) at 12 weeks, most highly significant ($p<0.001$) at 24 weeks & at 36 weeks, indicating the fact that there was significant rise in HDL was seen by medication.
- In combined group, Z test was applied for testing the effect on increasing HDL. Z test applied was insignificant ($p>0.05$) at 12 weeks, but most highly significant ($p<0.001$) at 24 weeks & 36 weeks, indicating the fact that there was delayed but significant steady rise in HDL at 24 weeks & 36 weeks of medication.

For Triglycerides level

- In Metformin group, Z test applied was insignificant ($p>0.05$) at 12 weeks, significant at 24 weeks & 36 weeks, indicating the fact that there was significant decreasing effect of Triglycerides by the medication and the level of Triglycerides is reduced steadily.

- In Sitagliptin group, Z test applied was insignificant at 12 to 24 week, but then become significant at 36 week indicating the fact that there was little reduction in Triglycerides initially and which remained significant from 24 to 36 weeks of initiating medication.
- In Combination group, Z test applied was not significant ($p>0.05$) as there was some rise followed by some fall due to large Variation (S.D).

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