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Original Research Article

A COMPARATIVE STUDY TO EVALUATE THE EFFECTS OF SITAGLIPTIN MONOTHERAPY VS SITAGLIPTIN + METFORMIN COMBINATION THERAPY ON BODY MASS INDEX, HDL CHOLESTEROL AND SERUM TRIGLYCERIDE LEVELS.

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ABSTRACT

Objectives: To compare the effects of combination of sitagliptin + Metformin vs Sitagliptin alone on paramaters such as Body mass index, HDL-C & Triglyceride levels in recently diagnosed patients of type 2 Diabetes mellitus.

Methods: This is a cross-sectional study which includes evaluation of body mass indices and biochemical parameters of 50 patients divided in 2 groups of 25 subjects in each group. Group 1 is Sitagliptin only group (100 mgs given in two divided dose of 50 mg each orally) and Group 2 is Metformin 1000 mg + Sitagliptin 50 mg given twice a day . Their body weight (BMI) were calculated & and biochemical parameters pertaining to lipid profile 1) HDL choleterol & 2) serum Triglycerides were measured and findings were recdorded at base line and in each follow-up. Z test is used for statistical analysis.

Results: Results are reported as either statistically significant or not .From 24th week onwards there was statistically significant reduction in BMI in both the groups more so of in the Group 2 (Combination group) where the reduction in BMI was highly significant ($p<0.001$). The HDL choleterol level showed an increment which was significant in both the groups in group 2 it was highly significant ($p<0.001$). Triglyceride levels in Sitagliptin alone group showed significant reduction whereas sitagliptin + metformin combination group showed slight increase in triglyceride levels the difference was significant.

Conclusions: In conclusion, significant differences was found in body mass index, HDL cholesterol levels and serum triglyceride levels in type 2 DM patients treated either with sitagliptin alone or in combination with metformin. Furthermore the reduction in body mass index and elevation in levels of HDL cholesterol were more in Combination drug treatment group as compared to sitagliptin alone.

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1. INTRODUCTION

South Asia, home to nearly a quarter of the world's population, is currently undergoing an epidemiological transition with an explosion in the prevalence of non-communicable diseases (NCDs). India, the largest country in the region, is also the largest contributor to the NCD burden. Type 2 Diabetes mellitus (DM),falls in the spectrum of NCD's and is a widespread endocrine metabolic disorder, is an important cause of morbidity and mortality worldwide also. India is currently diabetic capital of the world with 101 million cases of diabetes and 136 million of prediabetic cases being reported(17).The burden of Type 2 Diabetes Mellitus (T2DM) in India is massive, and with 77 million people, the country ranks second for having the highest number of T2DM patients in the world, following China (18) 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 and decresed beta cell function .[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

The aim of this study is to compare the effects of combination of sitagliptin + Metformin vs Sitagliptin alone on paramaters such as Body mass index, HDL-C & Triglyceride levels in recently diagnosed patients of type 2 Diabetes mellitus.

2. MATERIALS AND METHODS

A total of 75 subjects were studied & all investigations were carried out. Out of these subjects, 50 subjects regular in follow up were selected for the study. Follow-up was done regularly and data were collected at baseline that is at the 0^{th} day i.e the day of enrollment, 12weeks, 24 weeks and at 36 weeks. They were divided into two groups of 25 patients each.

Group 1 received sitagliptin alone in an oral dose of 50mg twice a day whereas

Group 2 received sitagliptin 50 mg + Metformin 1000mg twice a day.

Body weight in kgs and height in meters were recorded subsequent to which body mass index was calculated as BMI = weight (kg) / [height (m)]^2 . Also random venous blood sample were taken and analyzed for lipid profile parameters namely serum HDL cholesterol and serum triglycerides in both the groups.

Thus a total of three Parameters were observed

A) BODY MASS INDEX – BMI
B) SERUM HDL CHOLESTEROL
C) SERUM TRIGLYCERIDES

Informed consent was obtained from subjects enrolled in the study. The subjects was given a choice of leaving the study in between. Enrolment of subjects in the study was initiated after ethical clearance from ethical committee of BRD Medical College, Gorakhpur

Inclusion criteria:

The Patients with raised FFBS level >= 126mg/dl as per WHO guidelines for diagnosis of Diabetes Mellitus (recorded for the very first time) and confirmed by medical history were classified as recently diagnosed type 2 diabetics for the purpose of this study and included in the study.

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Exclusion criteria:
Patients with type 1 diabetes mellitus, Individuals with type 2 diabetes mellitus taking other oral hypoglycemic agents since many years & who are on insulin therapy or having drug induced hyperglycemia & Pregnant females were excluded from the study.

Statistical analysis
Statistical comparison was done in both the groups with the baseline values.
Z test employed used for statistical analysis. Various p values were obtained. For $p>0.05$ was considered insignificant, whereas $p<0.05$ was considered to be significant, $p<0.01$ was considered more significant and $p<0.001$ was considered most significant.
As the same group was compared for follow up values with baseline values of the parameters so sample size for baseline values was designated as n1 and sample size for follow up values was taken as n2 since no loss to follow up was noted therefore n1=n2 and total sample size was n1+n2 therefore Z test was employed for sample size was >30.

3. RESULTS

The results reflected the efficacy of the administered medications. Statistically significant reduction in BMI were observed in both the groups after 24th week, but the in the group receiving combination of Metformin & Sitagliptin the reduction in BMI was statistically most significant ($p<0.001$).

Table 1: Mean± S.D. of BMI of the treatment groups

Groups	**Duration**			
	0-Week	**12th Week**	**24th Week**	**36th Week**
Group1 Sitagliptin 50mg BD	26.14±2.92	25.5±2.53	24.54±2.34	23.58±2.74
P value:-		p>0.05	p<0.05	p <0.05
Group2 Sitagliptin 50mg + Metformin 1000mg BD	26.54±2.05	25.58±1.99	24.62±1.79	23.98±1.29
P value:-		p>0.05	p<0.01	p<0.001

HDL-Cholesterol level was increased significantly ($p<0.01$) in both groups but in the combined treatment group i.e group 2 it was highly significant ($p<0.001$) observed from 24th week onwards.

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Table 2: Mean± S.D. values of HDL of the two groups

Groups	**Duration**			
	0-Week	**12th Week**	**24th Week**	**36th Week**
Group1 Sitagliptin 50mg BD	33.16±3.99	36.68±4.22	38.6±3.92	39.24±4.25
P value		p<0.01	p<0.001	p<0.001
Group 2 Sitagliptin 50mg + Metformin 1000mg BD	33.8±5.05	36.04±6.12	39.56±4.36	40.84±5.12
P value		p>0.05	p<0.001	p<0.001

The Triglyceride levels, in Sitagliptin only, group of patients showed significant (p<0.01) reduction. Where as in the combined sitagliptin + metformin group it was significantly (p<0.001) raised but showed fluctuating trends.

Table 3: Mean± S.D. of Triglyceride of the two groups

Groups	**Duration**			
	0-Week	**12-Week**	**24-Week**	**36-Week**
Group 1 Tab Sitagliptin 50mg BD	171.72±28.97	161.32 ±24.07	161.32 ±19.06	156.48±24.98
P value:-		p>0.05	p>0.05	p<0.05
Group 2	205.0±46.51	205.3±61.43	232.34±59.72	219.56±54.08

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(Tab Sitagliptin 50mg + Metformin 1000mg) BD				
P value:-		p>0.05	P<0.001	P<0.001

4. DISCUSSION

This study was conducted in total of 50 patients to compare the effects of Siatgliptin as monotherapy vs sitagliptin in combination with metformin in reducing in Body weight and thereby body mass index & improvement in Lipid profile. i.e. HDL- & Triglyceride levels. A group of 50 patients were evaluated divided into two groups of 25 individuals in each group. Where each individual served as one's own control. Patients were subjected to 3 follow-ups. i.e. 12 weeks, 24 weeks, 36 weeks. On their 1st visit and upon subsequent follow ups, BMI was calculated & their blood investigations such as serum HDL & Serum Triglycerides level were carried out & findings were noted in specially prepared case history proforma.

The Results of our study is comparable to the studies conducted by Katsuyama et al.[2] which reported that Body weight and BMI in obese were significantly greater as compared to non-obese 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, on the similar lines Yanai et al.[3] found a significant reduction in body weight and body mass index from the baseline after 6 months ($p<0.01$).Also Seck et al.[4] reported that administration of oral Sitagliptin was associated with significant weight loss ($p<0.05$) (-1.6 kg) as against 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] obsereved, through multivariate regression analysis that after 52 weeks reduction in HbA1c was significantly associated with body mass index & other parameters. In another study, Amjad et al.[7] revealed significant difference in weight as well as other parameters for glycemic control in the two groups, of Sitagliptin+ Metformin & of 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 which is well tolerated.is as efficacious as glimepiride in reducing HbA1C and fasting blood sugar. It also causes reduction in weight.A study conducted by Demir S. et al.[8] had concluded that in patients exhibiting inadequate glycemic control, addition of a DPP-4 inhibitor as a second oral anti diabetic agent to Metformin monotherapy provides better glycemic control and does not cause weight gain. Also 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) ($p<0.001$).Many other comparative studies such as one 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.Contrary to findings of our study, a conducted by Shigematsu E. el al.[10] had

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shown that changes in 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 reported significant ($p<0.05$) reduction in triglycerides. Their results clearly indicate the beneficial effect of Metformin on lipid profile in type II diabetes 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.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. Whereas as Mervat M. et al.[16] had demonstrated the effect of Sitagliptin monotherapy on lipid profile and Results of their study revealed that Sitagliptin significantly ($p<0.01$) reduces TG. It was further stated that Sitagliptin as monotherapy is effective in treatment of dyslipidemia in newly diagnosed T2DM.

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