A PROSPECTIVE STUDY OF ADDITION OF SITAGLIPTIN TO METFORMIN VERSUS METFORMIN ALONE IN TYPE 2 DIABETES MELLITUS PATIENTS

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ABSTRACT

BACKGROUND

Various oral hypoglycaemic agent has been used for the treatment of diabetes mellitus. Out of that, metformin is a biguanide, which is commonly used for the treatment of diabetes mellitus and sitagliptin is an orally effective inhibitor of dipeptidyl peptidase IV, which indirectly increase the secretion of insulin by preventing degradation of GLP-1. Present study is designed to evaluate the efficacy of addition of sitagliptin with metformin in comparison with metformin alone.

MATERIALS AND METHODS

Subjects included in this study were randomised into two groups. Group A were given metformin 500 mg once daily and group B was given metformin 500 mg plus sitagliptin 50 mg. Both the group consists of 30 patients each. Before start of the study, various parameter like fasting plasma glucose, postprandial plasma glucose, glycosylated haemoglobin, HDL-C, LDL-C, TG total cholesterol, fasting plasma insulin, glycosylated haemoglobin and HOMA-IR were measured. All the patients were followed regularly and advice regarding diet and regular exercise was given. Fasting plasma glucose was measured every 15 days. All the patients were informed about hypoglycaemia and its presentation. Patients were asked to inform about any adverse experience. All the parameters were measured after 16 weeks of treatment.

RESULTS

Fasting plasma glucose in group A was reduced to 104.6 mg/dL from its basal value 156.45 mg/dL. In group B, the fasting plasma glucose was reduced to 90.10 mg/dL from its basal value 154.7 mg/dL. Fasting plasma insulin in group A was 12.65 mIU/dL, which has been changed to 11.46 mIU/dL after 16 weeks of treatment with metformin 500 mg once daily. Fasting plasma insulin in group B has been decreased from basal value 13.24 mIU/dL to 12.46 mIU/dL at the end of 16 weeks. Glycosylated haemoglobin in group A was 7.64 at the start of study, which was decreased to 6.0 after 16 weeks treatment with metformin similarly in group B HbA1c was decreased from basal value 7.86 to 5.8 after 16 weeks of treatment. The HOMA-IR value also decreased in both group. In group A, initial value was 4.69, which was reduced to 2.94; and in group B, after 16 weeks, the basal value of 7.86 was reduced to 2.77.

CONCLUSION

Diabetes mellitus is a chronic progressive disease responsible for damage of major organ system. In present study, we have found that BMI and glycaemic index was improved when sitagliptin was added to metformin. Insulin resistance was better improved in sitagliptin combination group metformin alone. Sitagliptin addition is associated with increase in HDL-C.

KEYWORDS

Sitagliptin, Metformin, Type 2 Diabetes Mellitus.

HOW TO CITE THIS ARTICLE: Jawaharlal R, Maske PG. A prospective study of addition of sitagliptin to metformin versus metformin alone in type 2 diabetes mellitus patients. J. Evid. Based Med. Healthc. 2017; 4(73), 4327-4330. DOI: 10.18410/jebmh/2017/861

Financial or Other, Competing Interest: None.
Submission 11-08-2017, Peer Review 17-08-2017,
Acceptance 06-09-2017, Published 08-09-2017.
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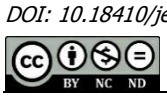
DOI: 10.18410/jebmh/2017/861



BACKGROUND

As per WHO data in 2015, India had 69.2 million people living with diabetes (8.7%). Of these, it remained undiagnosed in more than 36 million people.[1] Diabetes is a chronic disease that occurs either due to relative or absolute deficiency of insulin. Over the time, high blood sugar can seriously compromise every major organ system in the body causing heart attack, strokes, nerve damage, kidney failure, blindness, impotence and death.[1,2]

The goal of therapy in diabetes is to eliminate the symptoms of hyperglycaemia, reduce or eliminate the long-term complication and allow a patient normal lifestyle as possible.[3]

Various oral hypoglycaemic agent has been used for the treatment of diabetes mellitus. Out of that, metformin is a biguanide, which is commonly used for the treatment of diabetes mellitus and sitagliptin is an orally effective inhibitor of dipeptidyl peptidase-4, which indirectly increases the secretion of insulin by preventing degradation of GLP-1.[4]

Present study is designed to evaluate the efficacy of addition of sitagliptin with metformin in comparison with metformin alone.

MATERIALS AND METHODS

The present study was designed and carried out in the Department of General Medicine, Konaseema Institute of Medical Sciences, Amalapuram. The study protocol was approved by the institutional ethics committees and all the patients included in this study have provided written informed consent before start of the study. The study is conducted from February 2015 to June 2017. Total 60 patients were included in this study as per inclusion and exclusion criteria. All the patients were newly-diagnosed type 2 diabetes mellitus patients. For diagnosis of the patients, American Diabetes Association criteria was followed.[5] Subjects included in this study were randomised into two groups. Group A were given metformin 500 mg once daily and Group B was given metformin 500 mg plus sitagliptin 50 mg.

Both the group consists of 30 patients each. Before start of the study, various parameter like fasting plasma glucose, postprandial plasma glucose, glycosylated haemoglobin, HDL-C, LDL-C, TG total cholesterol, fasting plasma insulin, glycosylated haemoglobin and HOMA-IR were measured. All the patients were followed regularly and advice regarding diet and regular exercise was given. Fasting plasma glucose was measured every 15 days. All the patients were informed about hypoglycaemia and its presentation. Patients were asked to inform about any adverse experience. All the parameters were measured after 16 weeks of treatment. Hexokinase method was used for estimation of plasma glucose. For total cholesterol, we used Liebermann-Burchard reaction colorimetric method. Triglyceride was estimated by method of Neri and Fringe. HDL concentration was estimated by precipitation method. LDL concentration was calculated by WHO formula, LDL - cholesterol = total cholesterol - TG/5 - HDL (mg/dL).[6] Plasma insulin was determined by using enzyme-linked immunoabsorbent assay. HOMA-IR was calculated by using this formula (FPI X FPG)/22.5.[7]

Inclusion Criteria

- Newly-diagnosed patient.
- Both sex.
- Age below 30 to 60 yrs.
- FPG- 140 to 220 mg/dL.

Exclusion Criteria

- Complication of diabetes.
- Kidney and hepatic disease.
- Pregnancy and lactation.
- History of hypersensitivity to drug.

RESULTS

Total 60 nearly-diagnosed type 2 diabetes mellitus patients enrolled in this study as per exclusion and inclusion criteria and divided into two groups, each group having 30 patients.

To start with all the parameters were measured, and after 16 weeks of completion of treatment, all the parameters were repeated.

	Parameters Group A (n=30)			**Parameters Group B (n=30)**		
	Basal (Mean)	**After 16 wks. (Mean)**	**% Change in Mean**	**Basel (Mean)**	**After 16 wks. (Mean)**	**% Change in Mean**
Sex	22/8			20/10.		
Age (years)	52.4			54.2		
Body wt. (kg)	88.7	86.7	2.25	87.35	86.15	1.37
BMI (kg/m2)	30.6	30.18	1.37	31.3	30.46	2.87
FPG (mg/dL)	156.45	104.6	33.23	154.7	90.10	41.7
FPI (mIU/dL)	12.65	11.46	9.4	13.24	12.46	5.8
HOMA-IR	4.69	2.94	37.31	5.06	2.77	45.25
HbA1c	7.64	6.0	21.4	7.86	5.8	26.20
HDL (mg/dL)	38.60	44.2	14.50	36.4	42.4	16.48
LDL (mg/dL)	148.42	136.2	8.23	142.40	124.0	12.92
TG (mg/dL)	170	140.2	17.64	172.40	146.2	15.19
Total Chol. (mg/dL)	**264.2**	**220.2**	**16.66**	**258.4**	**210.2**	**18.68**
Measured Parameters						

In present study, the male-to-female ratio in group A was 22:8, and in group B, it was 20:10. Mean age of the patient in group A was 52.4 yrs., and in group B, it was 54.2 years. Mean body weight of patients in group A was 88.7 kg, which has been reduced to 86.7 kg after 16 weeks. In group B, the mean body weight was 87.35 kg, which was reduced to 86.15 kg. The body mass index in group A was 30.60 kg/m^2 has been reduced to 30.18 kg/m2 after 16 wks. Similarly, in group B, body mass index to start with, it was 31.3 kg/m^2 at the end of study.

Fasting plasma glucose in group A was reduced to 104.6 mg/dL from its basal value 156.45 mg/dL. In group B, the fasting plasma glucose was reduced to 90.10 mg/dL from its basal value 154.7 mg/dL. Fasting plasma insulin in group A was 12.65 mIU/dL, which has been changed to11.46 mIU/dL after 16 wks. of treatment with metformin 500 mg once daily.

Fasting plasma insulin in group B has been decreased from basal value 13.24 mIU/dL to 12.46 mIU/dL at the end of 16 weeks. Glycosylated haemoglobin in group A was 7.64 at the start of study, which was decreased to 6.0 after 16 weeks treatment with metformin similarly in group B HbA1c was decreased from basal value 7.86 to 5.8 after 16 weeks of treatment. The HOMA-IR value also decreased in both group. In group A, initial value was 4.69, which was reduced to 2.94, and in group B, after 16 weeks, the basal value of 7.86 was reduced to 2.77.

After 16 weeks of treatment and at the end of study, the lipid profile was also changed in both the groups. In group A, plasma LDL-C, which was 148.42 mg/dL in the start of the study decreased to 136.2 mg/dL in the end, and in group B, the nasal value of LDL-C was changed from 142.40 mg/dL to 124.0 mg/dL of 16 weeks of treatment. HDL-C concentration in group A was increased from 38.60 mg/dL to 44.2 mg/dL, and in group B, it was 36.40 mg/dL in the start of the study increased to 42.4 mg/dL after 16 weeks of treatment.

Total cholesterol level was also decreased from basal 264.2 mg/dL to 220.2 mg/dL in group A. In Group B, it decreased from basal value 258.4 mg/dL to 210.2 mg/dL. The triglyceride concentration in the start of the study was 170 mg/dL in group A after 16 weeks of treatment, it reduced to 140.2 mg/dL. In group B, basal value 172.40 mg/dL was reduced to 146.2 mg/dL.

DISCUSSION

In present study, we have evaluated the effect of addition of sitagliptin to metformin in comparison with metformin alone on newly-diagnosed type 2 diabetes mellitus patient.

We have observed the effect of metformin and metformin plus sitagliptin on body weight and BMI. We have found that, in group A, body weight was decreased by 2.25% of mean initial value; in group B, percentage change in mean was 1.37%, similarly % change in mean of wt. in group B was 1.37% and BMI was 2.87%.

Various studies has been conducted regarding effect of metformin on body weight and body mass index. As per A Golay et al, the metformin has variable effect on body weight,[8] but it does not allow increase in body weight. But, as per the study of Tiwari et al,[9] there was significant decrease in mean BMI, which support our study. Study of Shalini et al[10] shows that addition of sitagliptin is associated with significant decrease in wt. and BMI, which is similar to our study. In present study, we have found that percentage decrease in mean of FPG in group A was 33.23, and in group B, it was 41.7%, similarly the percentage change in mean value of glycosylated haemoglobin was 21.4% in group A and 26.20% in group B. These findings are consistent with the findings of Shalini et al.[10]

Hermansen et al reported that addition of sitagliptin is associated with reduction in FPG and HbA1c.[11] Ludvit et al reported that there is greater decrease in FPG when sitagliptin is added,[12] which is similar to our findings?.

It has been observed that in group B the percentage change in mean of insulin secretion was 5.8% in comparison with 9.4% in group A. HOME-IR value has decreased were in group B. So, even if the insulin secretion is not decreased, the insulin resistance has been improved in group B similar result was found by Derosa G et al.[13] Boahren et al[14] has reported that there is 41% HOMA-IR. In our study, the decrease in HOMA-IR was 45%.

In our study, we have found that addition of sitagliptin to metformin is associated with decrease in LDL-C, TG and total chol. and increase in HDL-C percentage, change in LDL concentration in group A and group B was 8.23% and 12.92%. Percentage change in mean Tg concentrate was 17.64% and 15.19%, respectively similarly. Total cholesterol reduction was more in group B than group A. HDL-C concentration was increased more in group B than group A. Shigenata et al[15] reported with decrease in Tg, LDL-C and total chol., which is similar to our study. Sakamoto Y et al[16] found that total cholesterol and triglyceride concentration fall after 12 weeks of treatment that also supports our study, but retrospective study of Horton does not support out finding HDL-C does not increase after 16 weeks of treatment.[17]

CONCLUSION

Diabetes mellitus is a chronic progressive disease responsible for damage of major organ system. In present study, we have found that BMI and glycaemic index was improved when sitagliptin was added to metformin. Insulin resistance was better improved in sitagliptin combination group metformin alone. Sitagliptin addition is associated with increase in HDL-C.

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