Improvement in lipid profile of the patients with saxagliptin as add on therapy to metformin in patients of type 2 DM who were previously on metformin alone with uncontrolled diabetes

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Abstract

Introduction: Diabetes is characterized by chronic hyperglycemia and disturbances of carbohydrate, lipid and protein metabolism. This study is an attempt to show an improvement in lipid profile (TC, TG, LDL and HDL) in patients of type 2 diabetes mellitus who were previously on metformin monotherapy with uncontrolled diabetes.

Material and method: A total of 30 patients were enrolled who were on metformin monotherapy and with uncontrolled diabetes. Patients were given metformin 500 mg twice a day and saxagliptin 2.5 mg once a day.

Patients were followed up at 1st, 3rd and 6th month and lipid profile (TC, TG, LDL and HDL) estimation was done during the follow up period.

Results: The mean age ± SD in male and female patients was 61.42 yrs ± 6.99 and 55.93 yrs ± 5.74 respectively. The mean change in value from baseline at 24 weeks was TC = 9.66%, TG = 9.40%, LDL = 14.87%, HDL = 5.63%. A highly significant difference has been seen at 0 v/s 1, 0 v/s 3 and 0 v/s 6 months in TC, TG, LDL and HDL values.

Conclusion: Saxagliptin has shown an improvement in lipid profile (TC, TG, LDL, HDL) during 6 months of treatment in patients of type 2 DM.

Keywords: Saxagliptin, Uncontrolled type 2DM, Metformin, Lipid profile.

Introduction

India had 69.2 million people living with diabetes (8.7%) as per the 2015 data. Of these, it remained undiagnosed in more than 36 million people.[1] The pathogenic processes involved in the development of diabetes range from autoimmune destruction of the β-cells of the pancreas with consequent insulin deficiency to abnormalities that result in resistance to insulin action. Long-term complications of diabetes include hypertension and abnormalities of lipoprotein metabolism - which causes increased incidence of atherosclerotic cardiovascular, peripheral arterial and cerebrovascular disease.[2] Elevated cholesterol levels, are believed to be a major factor in promoting atherosclerosis, it is now recognized that triglycerides are an independent risk factor. Atherosclerosis is characterized by the deposition of cholesterol from the plasma lipoproteins into the artery wall. In DM, prolonged elevated levels of VLDL, IDL, chylomicron remnants and LDL occur in the blood.[3] DM is reaching potentially epidemic proportions in India. The level of morbidity and mortality due to diabetes and its potential complications are enormous, and pose significant healthcare burdens on both families and society. Worryingly, diabetes is now being shown to be associated with a spectrum of complications and to be occurring at a relatively younger age. In India, the steady migration of people from rural to urban areas, the economic boom, and corresponding changes in lifestyle are all affecting the incident of diabetes. Yet despite the increase in diabetes there remains a paucity of studies investigating the precise status of the disease because of the geographical, socioeconomic, and ethnic nature of such a large and diverse country. Given the disease is now highly visible across all sections of society within India, there is now the demand for urgent research and intervention at regional and national levels to try to mitigate the potentially catastrophic increase in diabetes that is predicted for the upcoming years.

Materials and Methods

It was a randomized, prospective, comparative, interventional study conducted in the department of Pharmacology and department of Medicine at Dr. Rajendra Prasad Govt. Medical College, Kangra at Tanda after getting approval from Protocol review committee and Institutional Ethics Committee.

Inclusion criteria: Patients of age between 18 to 80 years with NIDDM, taking metformin in the doses of 1500 mg, having HbA1c level between 7% to 10% along with FPG levels 126 mg/dl and / or 2hPG 200 mg/dl were included in the study.

Exclusion criteria: Patients with

1. Acute complications of diabetes
   a. Hyperglycemic hyperosmolar state
   b. Diabetic ketoacidosis
2. Renal or liver disease.
3. Congestive heart failure.
4. Acute coronary syndrome.
5. Pregnancy

Methods

Total 30 patients were enrolled after screening for diabetes status with the help of HbA1C, FPG, PPPG. Detailed history taking, clinical examination and lab investigation including lipid profile (TC, TG, LDL, HDL) were done. Patients were given 500 mg metformin twice a day and 2.5 mg saxagliptin once a day. The patients were followed up at 1st, 3rd and 6th month. Lipid profile was repeated during each follow up.

Statistical analysis

At the end of 6th month, analysis was done using Microsoft excel version 2013.

Result

Total 30 patients were enrolled (14 males and 16 females). The mean age ± SD in male and female patients was 61.42 yrs ± 6.99 and 55.93 yrs ± 5.74 respectively.

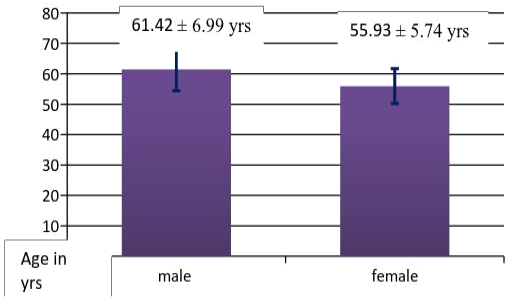


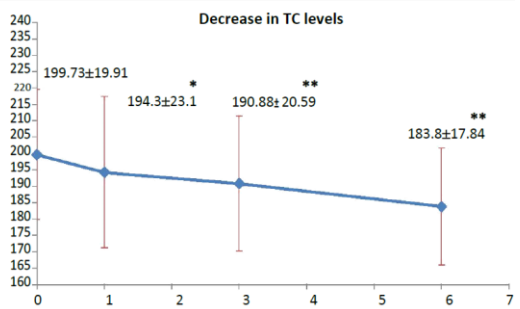
Fig. 1: Mean age ± SD in yrs.

Table 1: Changes in TC levels over a period of 6 months

Investigation	Duration (Month)	Saxagliptin (Mean ± SD)
	0	199.73 ± 19.91
TC	1	194.30 ± 23.10*
	3	190.88 ± 20.59**
	6	183.80 ± 17..84**

Unit – mg/dl, Normal value: < 200mg/dl

Mean change in TC from baseline at 24 weeks was 8.66%.



* P value 0.05 at 0 vs 1, and ** p < 0.001 at 0 vs 3 and 0 vs 6 months on intra group comparison

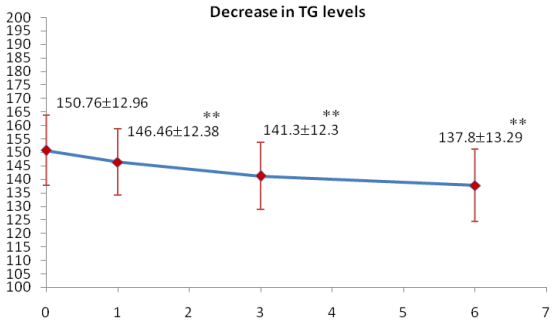
Fig. 2: Improvement in TC levels

Table 2: Changes in TG levels over a period of 6 months

Investigation	Duration (Month)	Saxagliptin (Mean ± SD)
	0	150.76 ± 12.96
TG	1	146.46 ± 12.38**
	3	141.30 ± 12.30**
	6	137.80 ± 13.29**

Unit – mg/dl, Normal value: <150 mg/dl

Mean change in TG from baseline at 24 weeks was 9.40%.



** P value 0.001 at 0 vs 1, 0 vs 3 and 0 vs 6 months on intra group comparison

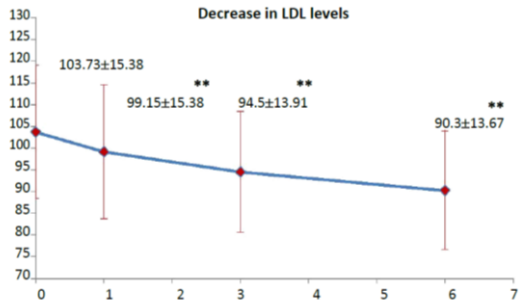
Fig. 3: Improvement in TG levels

Table 3: Changes in LDL levels over a period of 6 months

Investigation	Duration (Month)	Saxagliptin (Mean ± SD)
LDL	0	103.73 ± 15.38
	1	99.15 ± 15.38**
	3	94.50 ± 13.91**
	6	90.30 ± 13.67**

Unit – mg/dl, Normal value: 60-130 mg/dl

Mean change in LDL from baseline at 24 weeks was 14.87%.



** P value < 0.001 at 0 vs 1, 0 vs 3 and 0 vs 6 months on intra group comparison

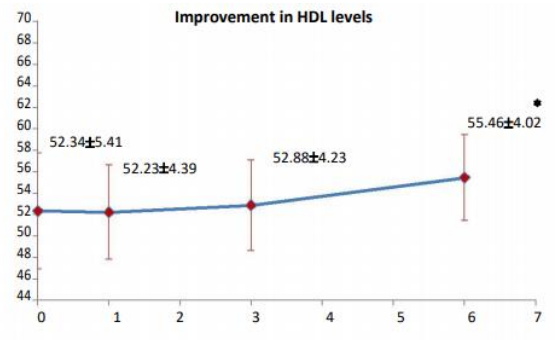
Fig. 4: Improvement in LDL levels

Table 4: Changes in HDL levels over a period of 6 months

Investigation	Duration (Month)	Saxagliptin (Mean ± SD)
HDL	0	52.34 ± 5.41
	1	52.23 ± 4.39
	3	52.88 ± 4.23
	6	55.46 ± 4.02*

Unit – mg/dl, Normal value: 30-65 mg/dl

Mean change in HDL from baseline at 24 weeks was 5.63%



* P value < 0.05 at 0 vs 6 months on intra group comparison

Fig. 5: Improvement in HDL levels

Discussion

It is well established that patients with type 2 diabetes mellitus (T2DM) are at increased risk of cardiovascular (CV) disease.[5,6] Therefore, it is important to consider the effects of glucose-lowering medications not only on glycemic control, but also on cardiovascular risk.[7,8] Saxagliptin belongs to dipeptidyl peptidase inhibitors which prevent deactivation of glucagon like peptide (GLP-1) and glucose dependent insulinotrpic polypeptide. Both GLP-1 and glucose dependent insulinotropic polypeptide are secreted from gut, they decrease glucose level by secreting insulin.

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