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Original Research Article.

Evaluation on Effects of Saroglitazar on HbA1c and Triglycerides on Patients with Type 2 Diabetes Mellitus: An Observational Study

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ABSTRACT

Saroglitazar has demonstrated significant reduction in triglycerides (TG) along with favorable effect on glycemic indices in diabetic patients. Our aim was to be the effects of saroglitazar on HbA1c and also on Triglycerides on patients with Type 2 diabetes mellitus. Analysis of glycemic parameters revealed a statistically significant 0.9% absolute reduction in HbA1c from baseline value of 8.23 % to 7.21% at 12 week follow-up. A significant reduction in fasting plasma glucose level of 23.5% from a mean baseline of 176.2mg/dL to mean follow-up value of 127.9mg/dL and a significant 26.2% mean reduction in post-prandial plasma glucose level from mean baseline level of 261.4 mg/dL to mean follow-up value of 184.2 mg/dL were observed. In conclusion, the use of saroglitazar 4 mg once daily for 12 Week is associated with significant improvement of lipid and glycemic parameters.

Key words: Saroglitazar, HbA1c, Triglycerides, Diabetic Dyslipidemia.

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INTRODUCTION

Although there has been tremendous research in the areas dealing with prevention and management of cardiovascular diseases, yet people with diabetes mellitus still have critically high morbidity and mortality subsequent to cardiovascular diseases.[1] Almost 80% of diabetic population have associative dyslipidemia (low high density lipoprotein (HDL), increased triglycerides (TG), and postprandial lipemia) which necessitates a drug therapy for treatment. This pattern is mostly seen in diabetes mellitus type 2 and may be a treat-able risk factor for consequent cardiovascular diseases.[2]

Diabetic dyslipidemia is an important factor contributing to the increased risk of The cardiovascular diseases.[3] Studies have shown that three out of four diabetes patients globally have associated dyslipidemia.[4] Diabetic dyslipidemia, also known as atherogenic dyslipidemia, is the triad of high triglycerides, higher proportion of small dense low density lipoprotein cholesterol and low high density lipoprotein cholesterol.[5] Currently statins, fibrates, niacin and omega 3 fatty acids are the available drugs in the armamentarium for the treatment of dyslipidemia. Saroglitazar is the novel molecule approved in India for the management of Diabetic dyslipidemia.

Saroglitazar is the world's first commercially available dual PPAR α and γ agonist which is approved for diabetic dyslipidemia and hypertriglyceridemia in type 2 diabetes not controlled by statin therapy. PPAR-α action of Saroglitazar improves lipid parameters and PPAR-γ action improves insulin sensitivity.[6] Saroglitazar, [(S)-a-ethoxy-4-{2-[2-methyl-5-(4-methylthio) phenyl)]- 1H-pyrrol-1-yl]-ethoxy})-benzenepropanoic acid magnesium salt], is the first glitazar to receive marketing approval and has been granted marketing permission in India in June 2013 in the name LipaglynH. At present it is available as 4 mg tablets. In clinical trials, saroglitazar has reduced triglyceride levels with modest reductions in HbA1c.[7] In previous studies, saroglitazar has shown significant benefit in terms of improvement in lipid and glycemic parameters with good safety profile. There has been a 46.7% decrease in TG, 32.5%decrease in non-HDL-C, 0.3% absolute reduction in glycosylated hemoglobin (HbA1c) with saroglitazar 4 mg in Indian Diabetic dyslipidemia patients.[7,8] This present observational study, we wanted to see the effects of saroglitazar on HbA1c and also on Triglycerides on patients with Type 2 diabetes mellitus.

MATERIALS AND METHODS

This present study was conducted in the department of Medicine, Heritage institute of medical sciences, Varanasi, Uttar Pradesh, India during the period from September 2016 to March 2017. The ethical clearance was taken from Heritage IMS, Varanasi. This observational study of saroglitazar in Indian diabetic patients who were on statin, i.e. either atorvastatin 10 mg daily or, rosuvastatin10 mg daily. Saroglitazar was prescribed in a dose of

4 mg daily, in accordance with approved guidelines, to patients with Type 2 diabetes and having hypertriglyceridaemia (serum triglyceride level >150 mg/dl).

Patients received treatment as par standard of care and no experiment was done on any patient. All patients were prescribed saroglitazar 4mg once daily for 12 weeks without changing the doses of on-going statin (i.e. either atorvastatin 10 mg daily or, rosuvastatin10 mg daily) therapy. Patients were evaluated for change in lipid parameters, glycemic parameters. Only data of patients with pre- and post-treatment values of fasting plasma glucose, post-meal plasma glucose, and HbA1c and serum lipid profile were taken into the study. The changes in laboratory parameters from baseline at 12 week follow up were statistically evaluated using paired "t" test.

RESULTS AND DISCUSSION

The data of 45 type 2 diabetes patients prescribed saroglitazar 4 mg once daily was recorded at baseline and at 12 week and analyzed. Out of 45 patients, 24 were male and 21 were female. The age of the patients was between 27 and 75 years and mean age was 49.24 years. All patients were advised to continue on-going statin (i.e. either atorvastatin 10 mg daily or, rosuvastatin10 mg daily) therapy and saroglitazar 4 mg once daily was prescribed as 2nd line lipid-lowering agent. Effect on blood glucose (Table 2): There were significant reductions in both fasting and post-prandial plasma glucose levels. There was also significant reduction in HbA1c level. However, it should be mentioned that antidiabetic medication was not changed, there was a modest and significant drop in HbA1c.

Table 1: Baseline patients' demographics parameters

Parameters	Baseline	After 12 weeks
Male (number)	24	-
Female (number)	21	-
Age Mean (yrs)	49.24	-
Weight Mean ± SD (Kgs)	68.14 ± 7.06	68.3 ± 7.0

Table 2: Change in lipid and glycemic parameters after 12 weeks follow up

Parameters	Baseline (Mean ± SD)	After 12 Weeks (Mean ± SD)	P- Value
Fasting plasma glucose (mg/dL)	176.2 ± 52.34	127.9 ± 32.17	<0.0001
Post-prandial plasma glucose (mg/dL)	261.4 ± 81.26	184.2 ± 47.25	<0.0001
HbA1c (%);	8.23 ± 1.58	7.21±0.25	<0.0001
Total Cholesterol (mg/dl)	158.08±48.46	148.51±36.74	<0.0001
TG (mg/dL)	345.77±245.01	152.02± 126.72	0.0001
HDL (mg/dL)	38.31±13.05	39.42±11.06	0.636
LDL (mg/dL)	87.83±15.83	83.65±14.15	0.0047

Analysis of glycemic parameters revealed a statistically significant 0.9% absolute reduction in HbA1c from baseline value of 8.23 % to 7.21% at 12 week follow-up. A significant reduction in fasting plasma glucose level of 23.5% from a mean baseline of 176.2mg/dL to mean follow-up value of 127.9mg/dL and a significant 26.2% mean reduction in post-prandial plasma glucose level from mean baseline level of 261.4 mg/dL to mean follow-up value of 184.2 mg/dL were observed (Table 2). Saroglitazar administration did not lead to weight gain. The mean body weight at baseline was 68.14 kgs and at 12 week follow-up was 68.3 kgs. No serious adverse events were reported (Table 1).

The recently published American College of Cardiology (ACC)/ American Heart Association (AHA) guideline on lipid management focussed on cardiovascular risk assessment and use of statins in patients with different categories of cardiovascular risk. The guideline also suggested avoiding medications or, supplements that may lower the cholesterol number but have no data to decrease cardiovascular risk.[9] Statins are recommended as the primary therapy for the management of dyslipidemia in diabetes by various guidelines like On November 26, 2013, the American Diabetes Association (ADA) posted a press release with comments on ACC/AHA guidelines on lipid management. ADA commented "Diabetes patients often have a unique pattern of dyslipidemia that may require specific consideration".[10] A recent review on effect of triglyceride on cardiovascular outcome analyzed various clinical trials between 1990 to 2008 and found uniform benefit of cardiovascular outcome of reduction of triglycerides with fibrates. Meta-analysis of subgroup of patients with a baseline triglyceride level of 2 mmol/L (178 mg/dl) or more, showed 43% risk reduction of lowering triglyceride by 1 mmol/L (89 mg/dl). The authors suggested a large cardiovascular outcome trial with patients with high triglyceride and normal HDLc level.[11] Saroglitazar, which is a dual PPAR alpha/gamma agonist has shown impressive results in clinical trials. At Week 12, saroglitazar 4 mg tablets significantly reduced mean plasma triglyceride levels by -46.7±3.02%, and the difference was significant (P<0.001) compared with placebo. Saroglitazar treatment was associated with a mean HbA1c reduction of 0.3%. Saroglitazar improves insulin sensitivity and it is a potent agent for controlling hypertriglyceridemia. Saroglitazar was found to be safe and well tolerated by patients.[7]

In our study, we have found more robust reduction in triglyceride and HbA1c. The probable reason was the baseline triglyceride was higher in our study and also possibly due to improvement in glycaemia that might have helped in reduction of triglyceride level. Saroglitazar, the only glitazar approved for clinical use, has shown

good efficacy and safety in short-term use. In our study, we have observed similar benefit on lipid glycemic parameters as found in clinical trails.

CONCLUSION

In conclusion, the patients with diabetic dyslipidemia, the use of saroglitazar 4 mg once daily for 12 Week is associated with significant improvement of lipid and glycemic parameters. Saroglitazar was safe, well tolerated and there was no serious adverse event reported.

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