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# Observational Study To Evaluate Effect of Saroglitazar in Indian Diabetic Dyslipidemia Patients

Medical Science

KEYWORDS : Saroglitazar, diabetes, dyslipidemia, Hypertriglyceridemia, PPAR

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## ABSTRACT

*Abstract-Saroglitazar is a peroxisome proliferation activated receptor α and γ agonist, approved in India for the management of diabetic dyslipidemia.*

*Aims: The study was to evaluate the effect of saroglitazar 4 mg once daily in diabetic dyslipidemia patients.*

*Methods: It was an observational study. Patients having type 2 diabetes, age above 18 years, having triglyceride ≥200 mg/dl were included.*

*Results: A total of 108 patients with mean duration of diabetes 5.65 years were included in this study. The baseline demographic profile was mean age 51 years, mean body weight 71.2 kg and mean BMI of 26.8 kg/m2. 53.2 % patients were male and 57.4 % were reported to be on statin therapy at baseline. All 108 patients were on antidiabetic medications at baseline. The baseline HbA1c value was 8.4 % and baseline triglyceride value was 322.3 mg/dl. At 3 months follow up, use of saroglitazar 4 mg led to reduction of TG (34.7 %), total Cholesterol (18%), LDL-C (16.8 %) and non-HDL (22.8%). Saroglitazar therapy lead to significant HbA1c reduction 0.8% with significant improvement in both fasting and post prandial blood glucose. There were no alteration in liver or renal enzymes, edema or weight gain were reported.*

*Conclusions: Saroglitazar can be used in type 2 diabetic dyslipidemia patients with Hypertriglyceridemia, not controlled alone by statin therapy, offering control of lipid and glycemic parameters with acceptable safety profile.*

## INTRODUCTION

Globally, the cardiovascular diseases (CVDs) burden is rising sharply and in present time is the most common cause of mortality. A major global study, INTERHEART study, identified nine easily measured risk factors [1] -

1. Smoking
2. Hypertension,
3. Lipids
4. Diabetes
5. Obesity
6. Diet
7. Physical activity
8. Alcohol
9. Psychosocial factors.

The above risk factors account for over 90 % risk of acute myocardial infarction. Dyslipidemia is the strongest risk predictor globally. Diabetic dyslipidemia is an important factor contributing to increased risk of cardiovascular diseases.[2] Many studies have shown that 75 % of diabetes patients globally have associated dyslipidemia.[3] Diabetic dyslipidemia is the triad of high triglyceride (TG), low high density lipoprotein concentration (HDL-C) and higher portion if small dense low density lipoprotein cholesterol (sd-LDL-C).[4] Statins, fibrates, niacin and omega 3 fatty acids are the available drugs for the treatment of diabetic dyslipidemia.

In India, Saroglitazar is approved for the management of diabetic dyslipidemia. Saroglitazar is the first dual peroxisome proliferator activated receptor which is both α and γ agonist. There has been a 46.7 % decrease in TG, 32.5 % decrease in non-HDL-C, 0.3 % absolute reduction in HbA1c with saroglitazar 4 mg once daily in Indian diabetes dyslipidemia patients.[5,6]

## METHODOLOGY

This was an observation study of saroglitazar 4 mg in Indian diabetes dyslipidemia patients. Saroglitazar 4 mg was approved in diabetes dyslipidemia having hypertriglyceridemia which was not controlled by statin therapy. Patients with type 2 diabetes, triglyceride level ≥ 200 mg/dl and age above 18 years were included in this study. The exclusion criteria were NYHA class III and IV heart failure, malignancy, pregnancy, lactating mother, active liver disease or patients having hypersensitivity with saroglitazar or any of the excipients used in formulations. The data were collected from the treating physicians who prescribed Saroglitazar from January 2013 to December 2013. In this study analysis, 131 patient data were obtained and those on antidiabetic medications were included in final analysis. Antidiabetic medications were not reported in 23 patients, hence only 108 patients were considered. All these 108 patients were prescribed tablet saroglitazar 4 mg once daily before breakfast. Patient's baseline and 3 month parameters- HbA1c, Fasting blood sugar, Post Prandial Blood Sugar, Total Cholesterol, LDL-C, HDL-C, TG, non-HDL-C and any adverse event if any were recorded. Non-HDL-C was obtained by deducting HDL-C from Total Cholesterol. Only those patients' data were considered which had baseline and three month follow up data (Out of 108 patients only 87 patients were data were used for analysis as they had both baseline and 3 months follow up recorded). The SPSS is used for data analysis. "p" value of < 0.05 was taken as significant.

**Table 1 Demographic profile of patients (N = 131).**

| |
|---|
| Age (years); n =131<br>51 ± 8 |
| Male 70 (53.4%) |
| Weight (kg); n = 131 71.2 ± 8.97 |
| BMI (kg/m2); n = 131 26.8 ± 3.27 |
| Average duration of diabetes (years);<br>n =131<br>5.65 ± 5.92 |

Data are mean ± SD values or number (%) as indicated. Abbreviations: N = number of subjects in specified treatment; n = number of subjects at specified category; BMI = body mass index. Data Determined at baseline.

## RESULTS

The data of 131 patients prescribed on saroglitazar 4 mg once daily was recorded at baseline and at 3 months. All patients were type 2 diabetes with average duration of diabetes of 5.65 years. The mean age of the patient was 51 years and 53.4 % patients were male. The patients had a mean weight of 71.2 kg and a mean body mass index of 26.8 kg/m$^2$. Out of 131 patients, 21 were reported to have history of coronary artery disease.

In this study 57.3 % of patients were reported to be on statin therapy, with atorvastatin being the most commonly used statin

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(82.7 %), at the time of entry. All patients were advised to continue on-going statin therapy. Saroglitazar 4 mg once daily was prescribed as 2nd line lipid lowering agent.

**Table 2 Number of patients (%) with or without ongoing statin therapy at baseline (N =131).**

| |
|---|
| With statin 75 (57.3%) |
| Atorvastatin 62 (82.7%) |
| Rosuvastatin 13(17.33%) |
| Pitavastatin 0 (0%) |
| Simvastatin 0 (0%) |
| Pravastatin 0 (0%) |
| Without statin 56 (42.7%) |

Out of 131 patients, concomitant antidiabetic medications at baseline were recorded in 108 patients (82.4%) and only these patient data were utilized for further analysis. Saroglitazar 4 mg was given in addition to on-going single antidiabetic therapy in 18.5%, to on-going dual antidiabetic therapy in 53.7% and in addition to more than two on-going antidiabetic therapy in 28.1% of the patients. In the study population(n=108), metformin was the most commonly reported antidiabetic drug at baseline in 83.3% of the patients, followed by sulphonylureas in 65.7 %, gliptins in 34.3 %, alpha glucosidase inhibition 12.9 %, insulin in 9.8%, , GLP 1 agonist 0.9 %, Meglitinide analogs 0.9%, bromocriptie in 0.9 and thiazolidinenoses in 5.5 % ( Table 3)

Saroglitazar showed significant improvement in all lipid and glycemic parameters at 3 months back up. The mean baseline triglyceride was 322.3 mg/dL vs 210.46 mg/Dl at 3 month follow-up, a significant reduction of 34.7%. Non-HDL–C levels also reported a significant 22.8 % mean reduction at 3 months follow up. .A statistically significant improvement in all other lipid parameters was also noted (a mean reduction of 16.8 % in LDL-C levels, 33.2 % in VLDL-C level, 18% in Total Cholesterol levels and mean increase of 6.9 % in HDL-C levels).

Analysis of glycemic parameters reveled a statistically significant 0.8% absolute reduction in HbA1c from baseline value of 8.2 to 7.4 at 3 month follow up. A significant reduction in fasting blood glucose level of 22.8% from baseline of 181.2 mg/dL to mean follow up value of 139.89 mg/dL and a significant 38.4% mean reduction in post-prandial blood glucose level with comparison to mean baseline level of 294.3 mg/dL to mean follow up value of 181.2 mg/dL were observed.

Saroglitazar administration didn't lead to weight gain. The mean body weight at baseline was 71.2 kg and at 3 month follow up was 69.9 kg. No serious adverse events were reported.

## DISCUSSION

As per latest guidelines from all major bodies like American Heart Association and American Diabetic Association, statins are recommended as the primary therapy in the management of dyslipidemia in diabetes.[7,8] Various studies have shown that Indians have higher TG level and low HDL-C as comparison to Caucasians.[9]

**Table 3 Pattern of baseline antidiabetic therapy.**

| |
|---|
| a. Number of patients (%) with or without on-going antidiabetic therapy (N =131) |
| Patients with antidiabetic therapy 108 (82.4%) |
| Patients without antidiabetic therapy 23 (17.6%) |
| b. Number of patients (%) with single, dual or more than two antidiabetic drugs (n =108) |
| Single antidiabetic drug 20(18.5%) |
| Dual antidiabetic drug 58 (53.7%) |
| More than two antidiabetic drugs 30 (27.8%) |
| c. Pattern of antidiabetic drug; (n =108) |
| Metformin 90 (83.3%) |
| Sulphonylureas 71 (65.7%) |
| Gliptins 37(34.3%) |
| Alpha glucosidase inhibitors 14 (12.9%) |
| Insulin 11 (10.2%) |
| Thiazolidinediones 6 (5.5%) |
| Meglitinide analogs 1 (0.9%) |
| GLP 1 agonist 1 (0.9%) |
| Bromocriptine 1 (0.9%) |
| *Data as number of patients (%). |

High TG is a major risk for Cardio Vascular Disease. A recent observational study in more than 75,000 subjects followed from general population, followed up for 34 years has revealed that lower TG level was associated with lower CV risk.

As per latest guidelines of American Association of Clinical Endocrinology (AACE) dyslipidemia guidelines when TG is above 200 mg/dL but <500 mg/dL recommend a non-HDLC calculation rather than LDL-C calculation for better risk assessment especially in insulin resistance.[12] The AACE diabetes guidelines suggest that non-HDL-C goal is to be achieved by TG lowering therapy after achievement of desirable LDL-C level.[13]

Meta-analysis of the five major trials on fibrates has shown 35% statistically significant decrease in coronary artery disease with fibrates in the group with subjects having baseline TG 204 mg/dL and HDL-C 34 mg/dL.[10,11] Thus there is increasing evidences by guidelines supporting the control of TG to target non-HDL-C and cardiovascular risk. At present the available options for the treatment of high TG are fibrates and niacin, associated with several side effects due to which their use is limited. The use of fibrates is associated with higher side effects of muscle symptoms when given in conjunction with statins, increased risk of cholelithiasis, and alteration in renal and liver parameters. Niacin is associated with decreased patient compliance due to following side effects like skin flushes, and also manifests glucose intolerance. In this context, saroglitazar, a novel molecule, is a dual PPAR-a/g agonist, approved for the use of Diabetes Dyslipidemia. The present study shows that saroglitazar with statins led to a significant improvement in lipid parameters. At 3 month there was a significant reduction in TG of 34.7%, LDL-C of 16.8%, total cholesterol of 18% and non-HDL-C of 22.8%. Further, in patients (with average duration of diabetes of 5.65 years) on existing baseline antidiabetic medications, the addition of saroglitazar, showed a significant 0.8% absolute reduction in HbA1c and with significant improvement in fasting and post prandial blood glucose. There were no serious adverse events reported. There were no alteration in liver or renal enzymes. There were no edema or weight gain reported in this study.

### Limitations of the study

This study is not a randomized, controlled clinical trial. This analysis consist of data obtained from clinical practice. The data that were analyzed at a short duration of 3 month follow up.

In this study adherence could not be assessed. More randomized and controlled clinical trials with longer duration of follow up will be necessary.

### Conclusions

In patients with diabetic dyslipidemia with saroglitazar 4 mg once daily for three month is associated with significant improvement of lipid and glycemic parameters. Saroglitazar was found to be safe, well tolerated and there was no serious adverse event reported.

### Conflicts of interest

Author has none to declare.

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