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COMPARATIVE STUDY OF EFFICACY AND SAFETY OF SAROGLITAZAR AND FENOFIBRATE IN DIABETIC DYSLIPIDEMIC PATIENTS

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ABSTRACT

Introduction: Dyslipidaemia associated with diabetes is marked by hypertriglyceridemia and decreased levels of high-density lipoprotein cholesterol (HDL-C) and raised or normal levels of low-density lipoprotein cholesterol (LDL-C) in type 2 diabetes mellitus (T2DM). This study compared the efficacy and safety of saroglitazar and fenofibrate in diabetic dyslipidemic patients attending tertiary care hospital.

Materials and Methods: This was a prospective, randomized, comparative, intervention study conducted for a period of 3 months in the patients with diabetic dyslipidaemia attending a tertiary care hospital. Patients were allocated randomly into 2 groups. Group A received one Saroglitazar 4 mg tablet after breakfast in conjunction with their routine anti diabetic drugs whereas Group B patients received one Fenofibrate 200 mg tablet after breakfast along with their routine anti diabetic drugs. Lipid profile, fasting blood glucose (FBG) and HbA1c were examined in patients on day 0 and after completion of 12 weeks. Throughout the course of treatment, they were asked to report and record any adverse event.

Result: At week 12,TG, Total Cholesterol, LDL-C and HbA1C levels decreased significantly and HDL-Cincreased significantly from their respective baseline values in both groups. particularly, the Saroglitazar group showed a more profound decrease in HbA1c, TG, Cholesterol, LDL-C, FBS and profound increase in HDL-C compared to the Fenofibrate group. 1out of 30 patients in Group Areported mild adverse events while 4out of 30 patients reported mild adverse events in Group B.

Conclusion: Hence, adding Saroglitazar to the drug regimen of patients with Diabetic Dyslipidemia can result in significant improvements in glycemic and lipid parameters with the added benefit of minimal side effects, demonstrating the efficacy and safety of Saroglitazar in the treatment of Diabetic Dyslipidaemia when compared to Fenofibrate.

Keywords: Diabetes mellitus, Diabetic dyslipidaemia, Fenofibrate, Saroglitazar,

INTRODUCTION

Diabetes mellitus (DM) is one of the world's major chronic disorders, increasing morbidity and death.[1] The global prevalence of diabetes among adults was predicted to be 6.4% in 2010,

impacting 285 million people, and is expected to rise to 7.7%, affecting 439 million people by 2030. The number of diabetic patients in India was 62.4 million in 2011, and this figure is expected to climb to a stunning 101.2 million by 2030. [2]

Diabetic dyslipidemia is a frequent and clinically relevant metabolic disease defined by altered lipid levels in people with diabetes mellitus. [3] Diabetes increases the risk of cardiovascular problems, including coronary artery disease and stroke, which are leading causes of morbidity and mortality. [4]

Diabetes and dyslipidemia have traditionally been treated using a number of oral anti-diabetic agents (ADAs) and hypolipidaemic medicines [5]. Statins are barely effective for 20-30% of people with dyslipidemia. Fibrates and Niacin have both failed to bridge the therapeutic gap, owing to the former's myotoxicity and the latter's lack of effectiveness in all patients [6, 7]. To fill this gap in therapy, Peroxisome Proliferator-Activated Receptors (PPAR)-a/g agonists were created. These compounds potentially treat both dyslipidemia and hyperglycemia in DD. PPAR-a agonists (fenofibrate) and PPAR-g agonists (pioglitazone) are authorized to treat dyslipidemia and type 2 diabetes. However, the latter and their use are associated with complications such as fluid retention, weight gain, and congestive heart failure [8].

As a result, the study focused on developing a dual PPAR-a/g agonist with the goal of controlling both lipid and glycemic parameters while maintaining an appropriate safety profile. These dual agonists can activate both the PPAR-a and PPAR-g receptors. They assist manage not only lipid but also glycemic indices and lower the risk of weight gain caused by PPAR-g activation. This lack of weight growth was initially noticed with the usage of fibrates, which not only had hypolipidemic effects but also lowered body weight without reducing food intake [9].

Saroglitazar is the first licensed dual PPAR-a/g agonist for DD patients, and it has demonstrated effectiveness in improving both lipid and glycemic indices while maintaining an outstanding safety profile [10].

The current study compared the efficacy and safety of saroglitazar with fenofibrate in diabetic dyslipidemia patients attending tertiary care hospital.

MATERIALS AND METHODS:

A prospective, randomized, comparative, interventional study was conducted at Government Medical College in Kamareddy, Telangana, after taking written informed consent from the patients and Institutional ethical committee clearance for a period of 3 months.

Inclusion criteria:

Adult subjects of either gender, aged 40-70 years,Type 2 Diabetic Dyslipidemic patients with FPG ≥ 126 mg/dl, plasma triglyceride level >200 mg/dl and HbA1C ≥6.5 and ≤9, Patients being treated with either a sulphonylurea, metformin or both for diabetes, None of the patients received any hypolipidemic agent during the past six months.

Exclusion criteria:

Female patients who are pregnant or lactating, fasting plasma glucose (FPG) > 250mg/dl, LDL-C > 130 mg/dl, co-morbid cardiovascular, renal and psychiatric complications, co-administration of drugs that may interact with saroglitazar, fenofibrate or metformin or sulphonylurea and that affect lipid profile and glycaemic status.

A total of 60 patients were enrolled. Following screening, the patients were divided into two groups of 30 patients each, using a computer-generated random number. Group A patients were given one Saroglitazar 4 mg tablet after breakfast, in addition to their usual anti-diabetic medications, whereas Group B patients were given one Fenofibrate 200 mg tablet after breakfast.

Study procedure

Patients had physical and baseline laboratory examinations. Liver function test (LFT), kidney function test (KFT) and thyroid-stimulating hormone (TSH) examination were undertaken at

baseline and the patients with deranged LFT, KFT and TSH were excluded from the study. A pre-designed proforma was produced for each subject, which included pertinent history and investigations. The study was conducted for three months. Patients' lipid profiles, fasting blood glucose (FBG), and HbA1c levels were measured on day 0 and 12 weeks later. They were instructed to record and document any adverse events that occurred during the course of treatment. They were able to communicate via phone and were called once a month to ensure their well-being and compliance with recommended therapy and instructions.

Statistical analysis: Quantitative data were expressed in mean±standard deviation and the differences between two comparable groups were tested by Student's t-test (unpaired). Qualitative data were expressed in percentage and the statistical differences between the proportions were tested by Chi-square test. '*P*' < 0.05 was considered statistically significant.

RESULTS

A total of 60 diabetic dyslipidemic patients were randomly divided into two groups. Of these, 30 patients were included in Group A (treated with saroglitazar 4 mg/day) and 30 patients were included in Group B (treated with fenofibrate 200 mg/day)

More number of males are there in Group A & Group B. Mean age of the patients was 55.62 years in Group A and 57.43 years in Group B respectively. Mean BMI of the patients was 25.8±3.82 in Group A and 26.2±3.85 in Group B as shown in Table 1

Table 1: Demography of study population

Characteristic	Group A (n=30)	Group B (n=30)
Male (%)	25(83%)	23(77%)
Female (%)	5 (17%)	7(23%)
Age (years)	55.62±6.86	57.43±7.01
BMI (kg/m2)	25.8±3.82	26.2±3.85

Regarding laboratory data, lipid profile parameters, including TG (Triglycerides), LDL (Low-Density Lipoprotein), HDL (High-Density Lipoprotein), VLDL (Very Low-Density Lipoprotein), and total cholesterol levels, and Fasting blood sugar (FBS) and HbA1c levels were shown in Table 2

Table 2: Laboratory data of patients

Laboratory data	Group A (Week 0)	Group B (Week 0)
TG (mg/dL)	238.4 ± 31.8	242.6 ± 32.8
LDL (mg/dL)	118.3 ± 8.24	117.3 ± 9.84
HDL (mg/dL)	33.64±5.64	34.35±5.86
VLDL level (mg/dL)	50.35±7.31	52.12±7.12
Cholesterol (mg/dL)	208.28±19.83	210.64±20.24
FBS (mg/dL)	162.62 ± 5.3	164.71 ± 6.8
HbA1c (%)	7.2 ± 0.5	7.14 ± 0.6

After treatment, TG, Cholesterol, LDL-C, FBS and HbA1C levels significantly decreased and HDL-C increased significantly from their respective baseline values in both groups. particularly, the Saroglitazar group showed a more profound decrease in HbA1c, TG, Cholesterol, LDL-C, FBS and profound increase in HDL-C compared to the Fenofibrate group at week 12 from their respective baseline values in both groups as shown in Table 3

Table 3: Comparison of lipid profile levels and blood sugar levels at the end of treatment

Laboratory data	Group A (Week 12)	Group B (Week 12)	p value
TG (mg/dL)	102.3 ± 7.45	112.8± 6.42	0.02*
LDL-C (mg/dL)	98.42±8.65	102.65±8.98	0.03*
HDL-C (mg/dL)	48.62±6.65	45±7.21	0.04*
VLDL-C (mg/dL)	34.13±6.76	37.24±5.97	0.6
Cholesterol (mg/dL)	161.65±17.23	171.87±18.54	0.002*
FBS (mg/dL)	88.14±7.02	112±8.02	0.03*
HbA1c (%)	5.62 ±0.53	6.72 ±0.45	0.01*

* Significance

The frequency of adverse effects, such as body pains, nausea, and gastritis, was assessed in each group. Overall, there were no significant differences in the frequency of adverse effects between the two groups. Group B had somewhat higher rates of body pains, nausea, and gastritis as compared to Group A as shown in Table 4

Table 4: comparison of side effects

Side effects	Group A (n=30)	Group B (n=30)	p value
Body ache	1 (3.3%)	2 (6.6%)	0.6
Nausea	0	1 (3.3%)	0.4
Gastritis	0	1(3.3%)	0.08

DISCUSSION

Dyslipidaemia is becoming increasingly common among persons with type 2 diabetes across the world. Despite the availability of various oral ADAs and hypolipidemic medications, current treatment methods are limited. Treatment of DD with major hypertriglyceridaemia is far from ideal. Conventional treatments are ineffective in treating hypertriglyceridaemia, and safety concerns exist. As a result, fresh therapeutic targets and medicines are always in demand. Saroglitazar is a dual PPAR-a/g agonist, the first glitazar licensed in the world, and has emerged as a new hope for efficiently treating DD with a low risk of adverse events, particularly without a rise in body weight [11].

In this 12-week research, we found that Saroglitazar 4 mg outperformed Fenofibrate 200 mg in terms of glycemic management and dyslipidemia control. The clinical studies PRESS V and PRESS VI demonstrated that saroglitazar reduced triglycerides. In the PRESS V research, saroglitazar considerably reduced FPG and HbA1C levels in a dose-dependent manner, which was comparable to the effectiveness of pioglitazone. There was also no significant change in body weights.[12] The PRESS VI research investigated saroglitazar in individuals with diabetic dyslipidemia who were not effectively managed with statins. The results of the PRESS VI research indicated that saroglitazar improved both lipid and glycemic markers.[13]

Safety analysis of our study demonstrated that saroglitazar 4mg had an excellent safety profile when compared to fenofibrate 200mg. Only one patient on saroglitazar reported having body pain, but two patients on fenofibrate experienced body pain, one had gastritis, and one had nausea, which was consistent with the prior study. [14] None of the patients were removed from the study. There were no reports of major life-threatening AE.

CONCLUSION: Adding Saroglitazar to the medication regimen of patients with Diabetic Dyslipidemia can result in a notable improvement in their glycemic and lipid parameters, along with the added benefit of negligible side effects. This indicates that Saroglitazar is more effective and safe than Fenofibrate in treating Diabetic Dyslipidemia.

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