

Rosuvastatin plus fenofibrate in diabetic dyslipidemia: a hospital record based study

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ABSTRACT

Background: Cardiovascular diseases (CVD) are the leading cause of death throughout world population each and every year. Focus on dyslipidemia management is urgently required in India to halt the rising tide of CVD. The purpose of diabetic dyslipidemia study is a record based one, to find out the effect of Rosuvastatin plus Fenofibrate, in adult Type 2 diabetes with dyslipidemia, with high TGL/HDL ratio in Lipid profiles, in a tertiary care hospital in the Union territory of Puducherry.

Methods: There were 101 patients hospital records were analysed in which male were 45 and females were 56. The various biochemical parameters like serum Total Cholesterol, HDL, LDL, TGL, Non-HDL, TCL/HDL Ratio and TGL/HDL ratio reports were collected before and after 12-weeks of Rosuvastatin 10 mg with Fenofibrate 145 mg combination, for the treatment period once daily for their lipid-lowering therapy.

Results: The combination therapies of Rosuvastatin plus Fenofibrate were safe and feasible to achieve more TG goal and proved that has predominately decreased the elevated lipid profiles from the medical resources of our record based study. The use of combination medications of rosuvastatin (10mg) plus Fenofibrate (145mg) is often needed to effectively treat the lipid triad, by the potency of rosuvastatin to lower LDL-C and Fenofibrates effectiveness in lowering TG in treating mixed diabetic dyslipidemia.

Conclusions: After Rosuvastatin (10mg) plus Fenofibrate (145mg), the lipid profile data proved that the importance of TGL/HDL ratio apart from the TCL/HDL ratio, for good lipid control in diabetic dyslipidemic patients.

Keywords: Cardiovascular disease, Diabetic dyslipidemia, Fenofibrates, Rosuvastatin

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide.¹ According to the Centers for Disease Control, the CVD are the leading cause of death in U.S, more than 600,000 (~1 in 4) die of heart disease each year. CVD is the most common, killing >370,000 people annually.² Recent studies proved that high cholesterol is present in 25 to 30% of urban and 15 to

20% rural populations and the prevalence is lower than high income countries.³

Increase in cardiovascular risk and hypercholesterolemia are associated in modern lifestyles. In India, recently there is an alarming increase in the prevalence of CVD risk over the past two decades at a younger age than other populations, with lower HDL cholesterol; increase triglyceride levels.⁴ Focus on dyslipidemia management is urgently required in India to halt the rising tide of CHD.

Importance of TGL/HDL ratio apart from the TCL/HDL ratio, for good lipid control in diabetic dyslipidemic patients may prevent CVD. Hence, our study focuses on the hospital records of diabetic dyslipidemia patients on Rosuvastatin plus Fenofibrate therapy. The patient's biochemical parameters like serum Total Cholesterol, HDL, LDL, TGL, Non-HDL, TCL/HDL Ratio and TGL/HDL ratio were collected before and after 12-weeks of therapy. The purpose of the findings shall emphasize the importance of TGL/HDL ratio apart from the TCL/HDL ratio, for good lipid control in dyslipidemic patients. Clinic based management of dyslipidemias in India can be improved with better physician education, as well as patient empowerment for better cholesterol control.⁵

METHODS

This study was carried out in Aarupadai Veedu Medical College and Hospital, Puducherry, based on hospital records for the past one year (September 2017- to August 2018). Patients with diabetic dyslipidemia who were on Rosuvastatin plus Fenofibrate were taken up for the study. The study protocol was approved by Institutional research committee of Aarupadai Veedu Medical College and Hospital, Puducherry (IRC No: AV/IRC/2018/079 dated 03.10.2018). The subjects were men and women from 25-70 years of age, with Type 2 diabetes mellitus with dyslipidemia. From the selected patients the hospital records for various biochemical parameters like serum Total Cholesterol, HDL, LDL, TGL, Non-HDL, TCL/HDL Ratio and TGL/HDL ratio were collected in a systematic and computerized way. The above biochemical investigations were noted before and after 12-weeks of Rosuvastatin 10 mg with Fenofibrate 145 mg combination, for the treatment period once daily for their lipid-lowering therapy.

The inclusion and the exclusion criteria were as follows, the male and female diabetic patients having Body Mass Index (BMI) <36kg/m², glycemic control (HbA1C <7%), were included in the study. The patients with continuous or periodic use of corticosteroids, drug induced nephro toxicity, secondary causes of albuminuria such as obstructive renal disease, renal stone disease and acute urinary tract infection, known proteinuria / ketonuria patients, patient with severe T1DM complication, pre-existing macro-vascular condition and pregnant females or who had given birth within the preceding 6 weeks, malignancy, severe infection, respiratory disease and liver disorder were excluded from the study.^{6,7} Our study has a total number of 101 patients of which male were 45 and females were 56. Data from the Medical Record Department of the Institute were summarized as the number of observations, and the mean, standard deviation by analysis of variance (ANOVA).

RESULTS

The Table 1 to 8 results indicate the observational reports of before Rosuvastatin and Fenofibrates therapy; Table 9

shows the results of fixed dose combination of Rosuvastatin and Fenofibrates before and after therapy in adult diabetes with dyslipidemia patients. In this study pattern 101 patients data were collected, male 45 and females 56, the age group >25 was nil in both male and female. In between 30-40 age group males and females were 10 and 9 respectively, in 41-50 group 11 and 19, between 51-60 age group males 12 and females 15 above 61 range males 15 and females 10 (Table 1).

Table 1: Age group.

Age group	Number of cases in males	Number of cases in females
Male		
> 25	NIL	NIL
30-40	10	9
41-50	11	19
51-60	12	15
> 61	15	10

The total cholesterol levels are categorized in to three groups (Table 2), between 150-200 (mg/dl), 200-250 (mg/dl) and >250 (mg/dl). In between 150-200 (mg/dl) group the numbers of patients of males and females were 33 and 45 in between 200-250 (mg/dl) group 12 and 11 and >250 nil.

Table 2: Serum total cholesterol level.

Before treatment of Rosuvastatin and Fenofibrates		
Serum cholesterol level (mg/dl)	Number of cases in males (mg/dl)	Number of cases in females (mg/dl)
150-200	33	45
200-250	12	11
>250	Nil	Nil

According the Serum HDL level the patients were divided in to four groups (Table 3). In between 31-35 (mg/dl) the number of cases was nil, 36-40 (mg/dl) group the male and female were 16 and 50; between 41-45 (mg/dl) serum HDL level groups the male and female 29 and 6.

Table 3: Serum HDL level.

Before treatment of Rosuvastatin and Fenofibrates		
Serum HDL level (mg/dl)	Number of cases in males	Number of cases in females
31-35	Nil	Nil
36-40	16	50
41-45	29	06
>45	Nil	Nil

Based on the Serum LDL level (mg/dl) the patients were divided in to four groups (Table 4) in which <100 (mg/dl) male and female one in each. Between 100-130 (mg/dl) group male 38 and female 43; in 131-160 (mg/dl) male 7 and female 11 and >160 (mg/dl) nil in each case.

Table 4: Serum LDL level.

Before treatment of Rosuvastatin and Fenofibrates		
Serum LDL level (mg/dl)	Number of cases in males	Number of cases in females
<100	1	1
100-130	38	43
131-160	7	11
>160	Nil	Nil

Serum TGL level of the patients were divided in to three groups (Table 5), <150 (mg/dl) the male and female were one in each; in 151-500 (mg/dl) males 44 and female 55, and >500 (mg/dl) nil.

Table 5: Serum TGL level.

Before treatment of Rosuvastatin and Fenofibrates		
Serum TGL level (mg/dl)	Number of cases in males	Number of cases in females
<150	1	1
151-500	44	55
>500	Nil	Nil

The Serum Non HDL level of the patients were divided in to three groups in first group <100 (mg/dl) the male and female were nil; in second group 101-130 (mg/dl) only one female and no male and third group >130 (mg/dl) category males 45 and females 55 (Table 6).

Table 6: Serum Non HDL level.

Before treatment of Rosuvastatin and Fenofibrates		
Serum Non HDL level (mg/dl)	Number of cases in males	Number of cases in females
<100	Nil	Nil
101-130	Nil	1
>130	45	55

Based on the Serum TCL / HDL <3.0 group both male and female were nil, in-between 3.0-4.5 group males 2 and females 1; in >4.5 group males 43 and females 55 respectively (Table 7).

Table 7: Serum TCL / HDL ratio.

Before treatment of Rosuvastatin and Fenofibrates		
Serum TCL / HDL ratio	Number of cases in males	Number of cases in females
<3.0	Nil	Nil
3.0 - 4.5	2	1
>4.5	43	55

The Serum TGL/HDL ratio (Table 8) shows that <3.0 group both male and females nil, and >3.0 group 45 males and 56 females were found.

Table 8: Serum TGL/HDL ratio.

Before treatment of Rosuvastatin and Fenofibrates		
Serum TGL/ HDL ratio	Number of cases in males	Number of cases in females
<3.0	Nil	Nil
>3.0	45	56

Before and after treatment of treatment of Rosuvastatin and Fenofibrates diabetes patients (Table 9). The Serum Total Cholesterol (mg/dl) was 196.03±8.72 and 169.82±10.23; the HDL (mg/dl) was 40.13±1.673 and 44.96±1.782; LDL (mg/dl) was 120.37±6.55 and 83.34±6.73, TGL (mg/dl) 179.68±13.58 and 158.94±15.204, non-HDL (mg/dl) was 156.47±8.07 and 122.48±8.734, the TCL/HDL ratio was 4.884±0.210 and 4.249±0.270 and TGL/HDL ratio 4.477±0.282 and 3.977±0.294 respectively.

Table 9: Results of the observational study fixed dose combination of Rosuvastatin and Fenofibrates before and after therapy- in adult diabetes with dyslipidemia.

Observations and biochemical parameters	Before treatment of Rosuvastatin and Fenofibrates	After treatment of Rosuvastatin and Fenofibrates
Serum total cholesterol (mg/dl)	196.03±8.72	169.82±10.23
HDL (mg/dl)	40.13±1.673	44.96±1.782
LDL (mg/dl)	120.37±6.55	83.34±6.73
TGL (mg/dl)	179.68±13.58	158.94±15.204
Non-HDL (mg/dl)	156.47±8.07	122.48±8.734
TCL/HDL Ratio	4.884±0.210	4.249±0.270
TGL/HDL Ratio	4.477±0.282	3.977±0.294

DISCUSSION

The standard lipid profile guidelines to treat patients with metabolic syndrome like diabetes the normal value includes serum Total Cholesterol 40-200 (mg/dl), HDL 45-65 (mg/dl), LDL (DM) 50-70 and (NDM) 70-100 (mg/dl), TGL 0-150 (mg/dl), Non-HDL (DM) <100 and (NDM) <130 (mg/dl), TCL/HDL ratio <3.0-4.5 and TGL/HDL ratio <3.⁸

In this study pattern 101 patients data were analysed based on age group (Table 1), serum Total Cholesterol (Table 2), Serum HDL level (Table 3), Serum LDL level (Table 4), Serum TGL level (Table 5), Serum Non HDL level (Table 6), Serum TCL / HDL ratio (Table 7) and Serum TGL/HDL ratio (Table 8).

According to the American Heart Association, young women have a much lower risk of cardiovascular disease due to the protective role of the hormone estrogens. Men 45 years or older are at a higher risk, and also younger men need attention too, further the American Heart Association

journal Circulation indicated that insulin resistance play a major role in the increased risk of Cardiovascular disorders for younger men. In this case females were more in number than males indicate that mixed diabetic dyslipidemia and also less sample size. The gender-related changes in insulin resistance in adolescents and found that insulin resistance was more frequent in males than females, despite leaner body types in the males.

In diabetes the insulin resistance is associated with a decrease in HDL and an increase in triglycerides.^{9,10} A high link between insulin resistances and atherosclerosis in Type 2 diabetes causes blood vessel disease. The treatment of Rosuvastatin and Fenofibrates has elevated the HDL cholesterol and decreased LDL cholesterol. The cluster of lipid abnormalities or the diabetic dyslipidemia associated primarily with Type 2 diabetes may be the cause of a high concentration of TG and LDL and low HDL cholesterol. The lipid abnormalities may be seen due to the unbalanced diet, high content saturated fats in the foods, excessive weight, lack of exercise, genes and also certain medications and medical conditions involving thyroid, might cause the patients at risk for premature atherosclerosis and coronary heart disease. It is quite common that atherosclerosis and blood vessel disease may develop even before diabetes is diagnosed.^{11,12}

The treatment of Rosuvastatin and Fenofibrates has altered the Serum Total Cholesterol, LDL, and TGL and subsequent gradual increase in HDL (Table 9). Lowering LDL has become a primary goal in cardiovascular prevention and commonly estimated from quantitative measurements of total and HDL-cholesterol and plasma triglycerides (TG) using the empirical relationship of Friedewald et al. And also, LDL has been associated with the development of plaque deposits on artery walls, which narrow the passage and restrict blood flow.^{13,14}

After the Rosuvastatin (10mg) plus Fenofibrate (145mg) treatment the TCL/HDL Ratio and TGL/HDL Ratio were decreased indicating a good lipid profile control (Table 9). The total cholesterol to HDL cholesterol ratio is a number that is helpful in predicting atherosclerosis, the process of fatty build-up in the walls of the arteries. The number is obtained by dividing total cholesterol by HDL cholesterol. A high ratio indicates a higher risk of heart attack while a low ratio indicates a lower risk. Non-HDL cholesterol is a strong marker of risk, an abnormal ratio of triglycerides to HDL-cholesterol (TG/HDL-c) indicates an atherogenic lipid profile and a risk for the development of coronary disease. Triglyceride/HDL cholesterol ratio (TG/HDL-C ratio) correlates strongly with the incidence and extent of coronary artery disease. It is a common phenomenon for both for men and women.¹⁵

It is common and generally acknowledged by the physician that, in daily practice Fenofibrates reduces TG levels to a greater extent than statins. And also, the TG level remains high after statins therapy in many patients with in the diabetes or metabolic syndrome. A

combination therapy with Fenofibrates and Rosuvastatin should be more effective than statins alone in reducing TG in the mixed dyslipidemia, characterized by a lipid triad of elevated triglycerides, elevated low-density lipoprotein-cholesterol and reduced high-density lipoprotein cholesterol in diabetes complication condition.^{16,17}

This study is an attempt to high light the outcomes of Rosuvastatin plus Fenofibrate in diabetic dyslipidemia. The importance of TGL/HDL ratio apart from the TCL/HDL ratio, for good lipid control in dyslipidemic patients from the a hospital record based study by following the "Third Report of the Expert Panel on detection, evaluation, and treatment of high blood cholesterol in Adults (Adult Treatment Panel III, or ATP III) presents the National Cholesterol Education Program (NCEP) updated recommendations on cholesterol testing and management".^{18,19}

Our record based survey fit in the new features of ATP III include, aggressive treatment of persons who are at relatively high risk for coronary heart disease due to multiple risk factors, Use of the lipoprotein profile as the first test for high cholesterol, a new level at which low HDL (high density lipoprotein) becomes a major heart disease risk factor, a new set of "Therapeutic Lifestyle Changes" to improve cholesterol levels, an increased focus on a cluster of heart disease risk factors knows as "the metabolic syndrome" and increased attention to the treatment of high triglycerides. Hence, the use of combination medications of Rosuvastatin (10mg) plus Fenofibrate (145mg) is often needed to effectively treat the lipid triad, by the potency of Rosuvastatin to lower LDL-C and Fenofibrates effectiveness in lowering TG in treating mixed dyslipidemia.

CONCLUSION

In conclusion, after Rosuvastatin (10mg) plus Fenofibrate (145mg), therapy the lipid profile of diabetic dyslipidemia patients the atherosclerotic vascular diseases and metabolic syndrome could be improved. The combination therapies of Rosuvastatin plus Fenofibrate were safe and feasible to achieve more TG goal in terms of medical resources from our record based study.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Research committee of Aarupadai Veedu Medical College and Hospital, Puducherry, India (IRC No: AV/IRC/2018/079 dated 03.10.2018)

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