ORIGINAL RESEARCH

Comparative Efficacy of Rosuvastatin and Ezetimibe Combination Therapy Versus Rosuvastatin Monotherapy on Lipid Profiles in Patients with Coronary Artery Disease

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ABSTRACT

Background: One of the main causes of death worldwide is coronary artery disease. The prevalence of cardiovascular diseases (CVDs) is rising in India and is posing a significant financial burden. The present study was conducted to compare the efficacy and safety of Rosuvastatin/ Ezetimibe combination therapy vs Rosuvastatin alone on the lipid profile of patients with CAD.**Materials & Methods:**100 patients of CAD of both genders were divided into 2 groups. Group I was started on rosuvastatin 10 mg once daily, and Group II was started on rosuvastatin 10 mg+ Ezetimibe 10 mg daily. The fasting serum lipid profile was repeated initially after 12 weeks and then after 24 weeks. All patients underwent routine investigations hemoglobin (Hb), random blood sugar (RBS), renal function test (RFT), liver function test (LFT), ECG and other investigations (cardiac biomarkers like CPK-MB and Troponins in patients presenting with chest pain) as required.**Results:**Group I had 26 males and 24 females and group II had 25 males and 25 females. In group I and group II, TC at baseline was 236.2 and 242.6, at 12 weeks was 156.8 and 150.4 and at 24 weeks was 154.0 and 146.2. The mean TG at baseline was 230.5 and 218.2, at 12 weeks was 186.4 and 150.4 and at 24 weeks was 172.4 and 142.0 respectively. LDL-C at baseline was 152.4 and 164.2, at 12 weeks was 90.6 and 78.2 and at 24 weeks was 84.2 and 70.4. HDL-C at baseline was 38.4 and 39.4, at 12 weeks was 41.2 and 42.0 and at 24 weeks was 42.3 and 43.6 respectively. The difference was significant ($P< 0.05$).**Conclusion:** Ezetimibe and rosuvastatin together can be used as a safe and effective treatment for high-risk CAD patients, particularly those whose target lipid levels cannot be reached by statin monotherapy.

Keywords: cardiovascular diseases, random blood sugar, renal function test

INTRODUCTION

One of the main causes of death worldwide is coronary artery disease. The prevalence of cardiovascular diseases (CVDs) is rising in India and is posing a significant financial burden. Dyslipidemia has been identified as one of the most significant modifiable risk factors for the development of CAD by the majority of large epidemiological investigations, including the Framingham Heart Study.[1] There is a causal link between elevated serum cholesterol and a higher risk of CAD. It has been demonstrated that lowering serum cholesterol levels is a successful therapeutic strategy that considerably lowers the

incidence of CAD.[2]

For high-risk individuals, the risk benefit is greater if lipid-lowering medication is initiated earlier in life. Additionally, it has been determined that decreased levels of High-Density Lipoprotein Cholesterol (HDL-C) and increased Low-Density Lipoprotein Cholesterol (LDL-C) values are risk factors for CAD. One important therapeutic strategy for both primary and secondary prevention in individuals with cardiovascular illnesses is the reduction of LDL-C levels. For patients with CAD, the majority of current guidelines advise aggressive and successful lipid-lowering medication. For patients with CVD, statins (HMG CoA Reductase Inhibitors) are the first line of treatment for dyslipidemias. Numerous extensive investigations have demonstrated their effectiveness over time in lowering serum cholesterol/LDL-C levels and enhancing overall cardiovascular morbidity and death.[3] Studies have shown that many patients may not reach therapeutic goals with statin therapy alone, even though these medicines significantly lower LDL-C levels when used as monotherapy. For individuals in such group, combination therapy using a statin and a non-statin medication is a therapeutic option.[4,5]Combination therapy of ezetimibe (10 mg per day) with statin blocks both the synthesis and absorption of cholesterol, thereby having a synergistic effect on lipid metabolism. Higher doses of statins may result in musculoskeletal or hepatic side effects.[6] Rosuvastatin is a high potency statin which has been shown to have higher lipid lowering effect than other statins like simvastatin or atorvastatin.[7]

AIM AND OBJECTIVES

Aim

To evaluate and compare the efficacy of rosuvastatin monotherapy versus a combination of rosuvastatin and ezetimibe in improving lipid profiles among patients with coronary artery disease (CAD).

Objectives

1. **Baseline Comparison**: Assess and compare baseline lipid parameters—Total Cholesterol (TC), Triglycerides (TG), Low-Density Lipoprotein Cholesterol (LDL-C), and High-Density Lipoprotein Cholesterol (HDL-C)—between the two treatment groups.
2. **Treatment Efficacy Over Time**: Monitor and compare the changes in lipid parameters at 12 and 24 weeks post-treatment initiation in both groups.
3. **Statistical Significance**: Determine the statistical significance of differences observed in lipid parameter changes between the two treatment regimens over the study period.

MATERIALS AND METHODS

Study Design

This was a prospective, randomized, open-label, comparative study conducted to evaluate the efficacy and safety of Rosuvastatin/Ezetimibe combination therapy versus Rosuvastatin alone on the lipid profile of patients with Coronary Artery Disease (CAD).

Study Population

The study included 100 patients diagnosed with CAD, who were of both genders and provided written informed consent to participate in the study.

Study Place

The study was conducted in the Department of General Medicine,Major S.D. Singh Medical College & Hospital, Farrukhabad, Uttar Pradesh, India in collaboration with Department of Pathology, Major S.D. Singh Medical College & Hospital, Farrukhabad, Uttar Pradesh, India, where participants were recruited from outpatient and inpatient departments.

Study Duration

The study was conducted over a period of two years, from January 2019 to December 2020, including patient recruitment, follow-up, and data analysis.

Inclusion Criteria

- Patients aged between 40–75 years diagnosed with CAD.
- Patients with dyslipidemia requiring statin therapy.
- Patients willing to comply with study procedures and follow-up visits.
- Patients who provided written informed consent.

Exclusion Criteria

- Patients with a history of hypersensitivity to statins or Ezetimibe.
- Patients with active liver disease or significantly elevated liver enzymes (ALT/AST > 3 times upper normal limit).
- Patients with severe renal impairment (eGFR < 30 mL/min/1.73m²).
- Patients with uncontrolled diabetes mellitus or other metabolic disorders.
- Pregnant or lactating women.
- Patients currently enrolled in another clinical trial.

Ethical Considerations

The study was conducted following ethical guidelines as per the Declaration of Helsinki. Ethical clearance was obtained from the Institutional Ethics Committee prior to the commencement of the study. Written informed consent was obtained from all participants after explaining the purpose, benefits, and potential risks of the study.

Pathologists play a crucial role in several aspects of the research process.

1. Lipid Profile Analysis

Clinical pathologists are responsible for overseeing the analysis of lipid profiles, which includes measuring levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides. These measurements are typically performed using automated analyzers, such as the Vitros 250 dry chemistry autoanalyzer, which operates on the principle of reflectance photometry. The accuracy and reliability of these tests are paramount, as they directly influence the assessment of the therapy's efficacy.

2. Quality Control and Validation

Ensuring the validity and reliability of laboratory results is a key responsibility of clinical pathologists. They implement rigorous quality control measures, including the use of internal quality control samples and adherence to standardized protocols, to maintain the integrity of test results. This process is essential for the accurate interpretation of lipid levels and for monitoring changes over the course of the treatment.

3. Monitoring Safety Parameters

Beyond lipid levels, clinical pathologists also monitor safety parameters by analyzing liver function tests, such as aspartate aminotransferase (AST) and alanine aminotransferase (ALT), as well as creatine kinase (CK) levels. These tests help detect potential adverse effects of the therapy on the liver and muscles, ensuring patient safety throughout the study.

4. Data Interpretation and Collaboration

Clinical pathologists collaborate closely with other medical professionals to interpret laboratory data in the context of the patient's overall health status. Their expertise aids in understanding the implications of changes in lipid profiles and liver function tests, contributing to informed decisions regarding the continuation or adjustment of therapy.

5. Contribution to Personalized Medicine

The insights provided by clinical pathologists support the development of personalized treatment strategies. By analyzing individual responses to therapy, they help tailor interventions to achieve optimal outcomes for patients with CAD.

Study Procedure

- **Baseline Assessment:** Data such as name, age, gender, and medical history were recorded. A thorough clinical examination was carried out.
- **Pre-treatment Investigations:** Routine blood investigations including haemoglobin (Hb), random blood sugar (RBS), renal function test (RFT), liver function test (LFT), electrocardiogram (ECG), and cardiac biomarkers (CPK-MB and Troponins in patients presenting with chest pain) were performed.
- **Grouping of Patients:**
  - **Group I (Control Group, n=50):** Patients were started on Rosuvastatin 10 mg once daily.
  - **Group II (Intervention Group, n=50):** Patients were started on Rosuvastatin 10 mg + Ezetimibe 10 mg once daily.
- **Follow-up and Lipid Profile Measurement:**
  - Fasting serum lipid profile, including Total Cholesterol (TC), Low-Density Lipoprotein (LDL-C), High-Density Lipoprotein (HDL-C), and Triglycerides (TG), was measured at baseline, after 12 weeks, and again at 24 weeks.
- **Adverse Effects Monitoring:** Patients were closely monitored for any adverse events such as muscle pain, liver enzyme elevation, or gastrointestinal disturbances.

Outcome Measures

1. **Primary Outcome:**
   - Reduction in LDL-C levels from baseline at 12 and 24 weeks.
2. **Secondary Outcomes:**
   - Changes in total cholesterol, HDL-C, and triglycerides.
   - Incidence of adverse drug reactions.

Statistical Analysis

- Data were analyzed using SPSS software (version 21.0).
- Continuous variables were expressed as mean ± standard deviation (SD) and categorical variables as percentages.

- Comparisons between groups were made using the unpaired Student's t-test for continuous variables and the chi-square test for categorical variables.
- A P-value < 0.05 was considered statistically significant.

RESULTS

Table 1: Gender wise distribution of patients

Groups	Group I	Group II
Drug	Rosuvastatin	Rosuvastatin 10 mg+ Ezetimibe
M:F	26:24	25:25

Table 1 shows that group I had 26 males and 24 females and group II had 25 males and 25 females.

Table 2: Assessment of lipid parameters

Parameter at baseline, 12 weeks, and 24 weeks for both Group I (rosuvastatin 10 mg) and Group II (rosuvastatin 10 mg + ezetimibe 10 mg):

Parameter	Duration	Group I (n=50)	Group II (n=50)	P value
Total Cholesterol (TC)	Baseline	236.2 ± 22.5	242.6 ± 24.1	0.02
	12 weeks	156.8 ± 20.3	150.4 ± 18.7	0.15
	24 weeks	154.0 ± 19.8	146.2 ± 17.9	0.12
Triglycerides (TG)	Baseline	230.5 ± 80.2	218.2 ± 75.4	0.01
	12 weeks	186.4 ± 60.3	150.4 ± 55.2	0.03
	24 weeks	172.4 ± 55.1	142.0 ± 50.1	0.05
LDL Cholesterol (LDL-C)	Baseline	152.4 ± 40.1	164.2 ± 42.3	0.04
	12 weeks	90.6 ± 30.2	78.2 ± 28.5	0.08
	24 weeks	84.2 ± 28.6	70.4 ± 26.7	0.10
HDL Cholesterol (HDL-C)	Baseline	38.4 ± 8.5	39.4 ± 9.1	0.05
	12 weeks	41.2 ± 9.3	42.0 ± 9.7	0.65
	24 weeks	42.3 ± 9.7	43.6 ± 10.2	0.54

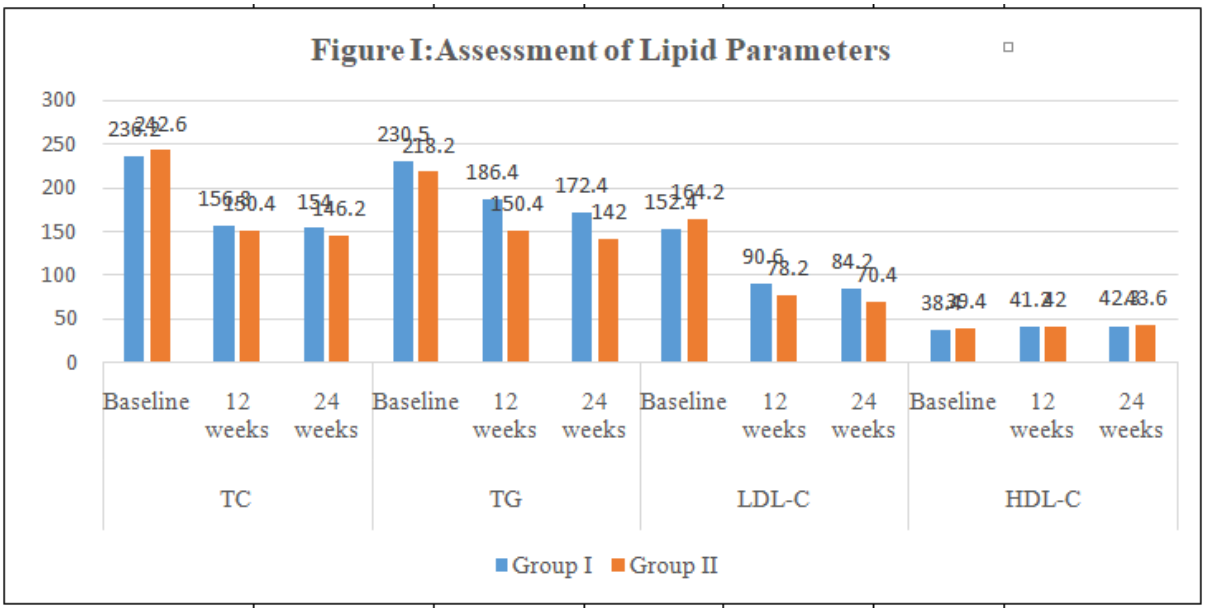

Table 2, figure I shows that Total Cholesterol (TC) at Baseline: Group I had a mean TC of 236.2 mg/dL, while Group II had 242.6 mg/dL (P = 0.02). 12 Weeks: Group I reduced TC to 156.8 mg/dL, whereas Group II reached 150.4 mg/dL. 24 Weeks: Group I's TC was 154.0 mg/dL, and Group II's was 146.2 mg/dL. Both groups showed significant reductions in TC, with Group II achieving a greater decrease.

Triglyceride at Baseline: Group I had a mean TG of 230.5 mg/dL, and Group II had 218.2 mg/dL (P = 0.01). 12 Weeks: Group I reduced TG to 186.4 mg/dL, while Group II reached 150.4 mg/dL. 24 Weeks: Group I's TG was 172.4 mg/dL, and Group II's was 142.0 mg/dL. Group II demonstrated a more pronounced reduction in TG levels compared to Group I.

Low-Density Lipoprotein Cholesterol (LDL-C) at Baseline: Group I had a mean LDL-C of 152.4 mg/dL, and Group II had 164.2 mg/dL (P = 0.04). 12 Weeks: Group I reduced LDL-C to 90.6 mg/dL, while Group II reached 78.2 mg/dL. 24 Weeks: Group I's LDL-C was 84.2 mg/dL, and Group II's was 70.4 mg/dL. Group II achieved a more significant reduction in LDL-C levels over time.

High-Density Lipoprotein Cholesterol (HDL-C) at Baseline: Group I had a mean HDL-C of 38.4 mg/dL, and Group II had 39.4 mg/dL (P = 0.05). 12 Weeks: Group I increased HDL-C to 41.2 mg/dL, while Group II reached 42.0 mg/dL. 24 Weeks: Group I's HDL-C was 42.3 mg/dL, and Group II's was 43.6 mg/dL. Both groups showed modest increases in HDL-C, with Group II having a slightly higher increase.

DISCUSSION

The primary line of treatment for dyslipidemias, particularly in patients with high-risk CAD, is statins. One option for these people is to use greater dosages of high-potency statins.[8] Studies assessing statin dosage uptitration discovered that while initial statin dosages could lower LDL-C by 20–30%, doubling the dose only produced a 5–6% further reduction.[9,10] Larger dosages also carry a larger chance of negative side effects. Using non-statin medications as an adjuvant therapy, like as ezetimibe, is an additional strategy.[11] The present study was conducted to compare the efficacy and safety of Rosuvastatin/ Ezetimibe combination therapy vs Rosuvastatin alone on the lipid profile of patients with CAD.

We found that group I had 26 males and 24 females and group II had 25 males and 25 females. Joshi et al[12] compared the efficacy and safety of Rosuvastatin/ Ezetimibe combination therapy vs Rosuvastatin alone on the lipid profile of patients with CAD in Northern India. The patients were randomly divided into age and sex matched two groups of 40 each. After baseline investigations and lifestyle modifications, Group I was started on rosuvastatin 10 mg once daily, while Group II was started on rosuvastatin 10 mg+ Ezetimibe 10 mg daily. The fasting serum lipid profile was repeated initially after 12 weeks and then after 24 weeks. The two groups were observed for side effects which were noted. combination therapy of rosuvastatin and ezetimibe resulted in significantly higher change in all lipid parameters (LDL-C, TC, TG, HDL-C) as compared to treatment with rosuvastatin alone. There was no difference in the adverse effects seen after treatment in the two groups.

We observed that in group I and group II, TC at baseline was 236.2 and 242.6, at 12 weeks was 156.8 and 150.4 and at 24 weeks was 154.0 and 146.2. The mean TG at baseline was 230.5 and 218.2, at 12 weeks was 186.4 and 150.4 and at 24 weeks was 172.4 and 142.0 respectively. LDL-C at baseline was 152.4 and 164.2, at 12 weeks was 90.6 and 78.2 and at 24 weeks was 84.2 and 70.4. HDL-C at baseline was 38.4 and 39.4, at 12 weeks was 41.2 and 42.0 and at 24 weeks was 42.3 and 43.6 respectively. In a study by Pearson TA et al.[13] including 769 patients of primary hypercholesterolemia, it was shown that by adding ezetimibe to the Statin therapy, significant reductions in LDL-C, TG and TC levels and increase in HDL-C level can be achieved. Also, 71.5% patients in combination group were able to achieve LDL-C target level as compared to only 18.9% in Statin-placebo group . Similarly, in the Ezetimibe Add-on to Statin for Effectiveness (EASE) trial, the combination therapy reduced the LDL-C level by an additional 25.8 % in the total population.

LIMITATIONS OF THE STUDY

- Small sample size (50 patients) limiting the generalizability of results.
- Open-label study design, introducing potential bias.
- Short follow-up duration (24 weeks), which may not capture long-term efficacy and safety outcomes.
- Single-centre study, limiting external validity.
- Lack of dietary and lifestyle assessment, which could impact lipid profile outcomes.

CONCLUSION

Authors found that Ezetimibe and rosuvastatin together can be used as a safe and effective treatment for high-risk CAD patients, particularly those whose target lipid levels cannot be reached by statin monotherapy.The combination therapy of rosuvastatin and ezetimibe demonstrated superior efficacy in improving lipid profiles compared to rosuvastatin monotherapy in patients with CAD. Specifically,

the combination therapy led to more significant reductions in TC, TG, and LDL-C levels, as well as a greater increase in HDL-C levels over 24 weeks. These differences were statistically significant ($P < 0.05$), indicating that adding ezetimibe to rosuvastatin enhances lipid-lowering effects. This combination therapy may be particularly beneficial for patients who do not achieve lipid targets with statin monotherapy or who experience side effects at higher statin doses.

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