ISSN(O) 3108-2246 https://doi.org/10.66328/ijprmh.2025.010103

International Journal of Public Research in Medicine and Health (IJPRMH)

Volume 1, Issue1, July-September, 2025

Original research Article

Comparative Efficacy and Safety of Daily Versus Alternate Day Dosing of Rosuvastatin in Dyslipidemic Patients: A Prospective, Randomized, Open Label Study

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Received: 19/08/2025
Revised: 10/09/2025
Accepted: 18/09/2025

Abstract

Background: Dyslipidemia is a major modifiable risk factor for atherosclerotic cardiovascular disease, and statins remain the cornerstone of therapy. Rosuvastatin is highly potent, but concerns regarding adverse effects and adherence have prompted evaluation of alternate dosing strategies.

Objective: To compare the efficacy and safety of daily versus alternate-day dosing of rosuvastatin in dyslipidemic patients.

Methods: In this prospective, randomized, open-label, parallel-group study, 90 patients with dyslipidemia were randomized into three groups: Group A (rosuvastatin 10 mg daily), Group B (rosuvastatin 10 mg administered alternately), and Group C (rosuvastatin 20 mg administered alternately). Patients were followed for 12 weeks with serial evaluation of lipid profile, glycemic parameters, and adverse events.

Results: All regimens significantly reduced total cholesterol, LDL-C, and triglycerides ($p < 0.001$), with no statistically significant differences between groups. LDL-C reduction approached 42% across all arms. HDL-C showed a modest, non-significant increase. HbA1c rose slightly but remained clinically insignificant; fasting blood sugar did not change meaningfully. Adverse events, mainly myalgia and headache, were more frequent with daily dosing, while alternate-day regimens were better tolerated. No serious adverse events occurred.

Conclusion: Alternate-day dosing of rosuvastatin provides lipid-lowering efficacy comparable to daily dosing, with fewer adverse events and potential cost savings. This regimen offers a safe and effective alternative for long-term dyslipidemia management in Indian patients. Larger and longer-term studies are needed to validate cardiovascular outcome benefits.

Keywords: Dyslipidemia, Rosuvastatin, Statins, Alternate-day dosing, Cardiovascular risk, India

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Introduction

Dyslipidemia, characterized by abnormal levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides, is a major modifiable risk factor for atherosclerotic cardiovascular disease (ASCVD) [1]. Elevated LDL-C levels, in particular, have been strongly linked with the initiation and progression of atherosclerosis, while reduced HDL-C is an independent risk factor for cardiovascular morbidity and mortality [2]. The global burden of dyslipidemia is substantial, and in India, rapid urbanization and lifestyle transitions have further amplified its prevalence, contributing significantly to premature coronary artery disease [3].

Statins, competitive inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, remain the cornerstone of lipid-lowering therapy. By reducing hepatic cholesterol synthesis and upregulating LDL receptors, statins lower LDL-C and improve cardiovascular outcomes [4]. Among them, rosuvastatin is notable for its high potency, longer half-life, and superior LDL-C reduction compared to other statins [5]. Clinical guidelines recommend daily statin therapy to achieve optimal lipid control; however, treatment adherence is often limited by statin-associated muscle symptoms (SAMS) and other adverse effects, which may reduce long-term compliance [6].

Alternative dosing strategies, such as alternate-day statin regimens, have been proposed to mitigate adverse effects while maintaining efficacy. Preliminary studies suggest that alternate-day rosuvastatin may achieve comparable lipid reductions to daily dosing, with improved tolerability in some patients [7]. Nonetheless, data specific to the Indian population remains scarce. Against this background, the present study was designed to prospectively evaluate the efficacy and safety of daily versus alternate-day rosuvastatin therapy in patients with dyslipidemia, aiming to identify an optimal dosing regimen that balances lipid-lowering efficacy with safety and patient adherence.

Materials and Methods

Study Design and Setting

This was a prospective, randomized, open-label, parallel-group, comparative clinical study conducted in the Department of Pharmacology, in collaboration with the Department of Medicine at the National Institute of Medical Sciences, Jaipur. The study duration was 12 weeks, including recruitment, intervention, and follow-up. The design was chosen to reflect real-world clinical practice and to evaluate both efficacy and safety of different dosing regimens of rosuvastatin in dyslipidemic patients.

Study Population

Patients were recruited from the outpatient department (OPD) of the Department of

Medicine at the National Institute of Medical Sciences, Jaipur. Both male and female patients aged 18–65 years with a confirmed diagnosis of dyslipidemia were screened. Dyslipidemia was defined according to the National Cholesterol Education Program (NCEP ATP III) criteria.

Inclusion Criteria

- Adults aged 18–65 years of either sex.
- Diagnosed cases of dyslipidemia (elevated LDL-C, TC, or TG, or low HDL-C).
- Willingness to provide informed consent and comply with study procedures.

Exclusion Criteria

- Patients who were unwilling to participate or provide informed consent.
- Current or recent (within 3 months) use of lipid-lowering agents.
- History of hypersensitivity to statins.
- Patients with uncontrolled diabetes mellitus (HbA1c >9%).
- Pregnant or lactating females.
- History of rhabdomyolysis or significant hepatic/renal dysfunction.
- Concurrent use of drugs known to interact with rosuvastatin (e.g., nicotinic acid, gemfibrozil, CYP3A4 inhibitors such as erythromycin, ketoconazole, cyclosporine, HIV protease inhibitors, amlodipine, or amiodarone).

Sample Size Calculation

The minimum sample size required was calculated to be 71, based on previously reported clinical trial data, assuming a study power of 80% ($\beta = 0.2$) and an α error of 5% ($p < 0.05$) to detect a clinically significant difference in LDL-C reduction between daily and alternate-day regimens. To account for attrition, 97 participants were recruited.

Randomization and Allocation

Participants were randomly assigned to three groups of equal size using a computer-generated random allocation sequence. Allocation concealment was ensured using sealed, opaque envelopes prepared by a pharmacist not involved in the trial. Ninety patients completed the study (7 patients were lost to follow-up).

Intervention Arms

- **Group A (n=30):** Rosuvastatin 10 mg orally once daily.
- **Group B (n=30):** Rosuvastatin 10 mg orally on alternate days.
- **Group C (n=30):** Rosuvastatin 20 mg orally on alternate days.

Study medications were provided as identical-appearing tablets to minimize perception bias. All participants were counseled on lifestyle modifications (dietary changes, exercise, and smoking cessation).

Study Procedures and Follow-up

At baseline, a detailed history (including demographic details, medical history, family history, and lifestyle factors) and a physical examination (including vital signs and BMI) were performed. Patients were followed at 4, 8, and 12 weeks. At each visit, compliance, adverse events, and concomitant medications were documented.

Laboratory Investigations

- **At baseline and week 12:** Lipid profile (TC, LDL-C, HDL-C, TG), fasting blood sugar (FBS), glycosylated hemoglobin (HbA1c).
- **At baseline, week 4, week 8, and week 12:** Hemoglobin, total leukocyte count (TLC), differential leukocyte count (DLC), urine routine, liver function tests (serum bilirubin, albumin, SGOT, SGPT, alkaline phosphatase), renal function tests (serum creatinine, blood urea).

All laboratory tests were performed in the central clinical laboratory of the hospital using standardized enzymatic methods (Cholesterol Oxidase Peroxidase for TC, Phosphotungstic Acid method for HDL-C, Friedewald's formula for LDL-C, and enzymatic kits for TG, HbA1c, and glucose).

Outcome Measures

- **Primary Outcome:** Percentage change in lipid parameters (TC, LDL-C, HDL-C, TG) from baseline to week 12.
- **Secondary Outcomes:**
  - Change in glycemic parameters (FBS, HbA1c) from baseline to week 12.
  - Frequency and nature of adverse events.
  - Tolerability and treatment discontinuations.

Safety Monitoring

Adverse events were recorded at each visit through structured questionnaires and spontaneous patient reporting. Muscle-related complaints (myalgia, cramps), hepatic or renal derangements, and other systemic symptoms were specifically probed. Serious adverse events (SAEs) were predefined as events requiring hospitalization or resulting in significant disability. No SAE occurred during the study.

Ethical Approval and Registration

The protocol was reviewed and approved by the Institutional Ethics Committee of Government Medical College, Amritsar, prior to patient enrolment. Written informed consent was obtained from all participants after explaining the study objectives, interventions, potential risks, and benefits in a language they understood.

Statistical Analysis

Data were analyzed using SPSS version 22. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were expressed as percentages. Intragroup comparisons

(baseline vs 12 weeks) were performed using a paired t-test. Intergroup comparisons were assessed by one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test. Categorical data were analyzed using Chi-square or Fisher's exact test as appropriate. A two-tailed p-value <0.05 was considered statistically significant.

Results

Table 1. Baseline characteristics of study participants (n=90)

Parameter	Group A	Group B	Group C	p-value
Age (years, mean ± SD)	52.1 ± 8.3	51.6 ± 7.9	50.8 ± 9.1	0.72
Male sex (%)	56.7	53.3	60.0	0.81
BMI (kg/m²)	26.2 ± 3.8	26.5 ± 4.1	25.9 ± 3.6	0.67
Hypertension (%)	43.3	40.0	46.7	0.88
Baseline TC (mg/dL)	234.5 ± 28.7	236.1 ± 30.4	231.9 ± 29.6	0.91
Baseline LDL-C (mg/dL)	151.7 ± 23.2	153.2 ± 25.1	149.6 ± 24.3	0.83
Baseline HDL-C (mg/dL)	39.2 ± 5.4	38.6 ± 5.9	39.8 ± 6.1	0.76
Baseline TG (mg/dL)	178.4 ± 35.7	181.2 ± 33.9	175.6 ± 36.1	0.69

Table 1 shows the baseline demographic and clinical characteristics of the study participants. There were no statistically significant differences among the three groups in terms of age, sex distribution, BMI, prevalence of hypertension, or baseline lipid levels, indicating successful randomization and comparability at the study's outset.

Table 2. Lipid profile changes within groups (baseline vs 12 weeks)

Parameter	Group A Δ (%)	Group B Δ (%)	Group C Δ (%)	p (within)
TC	-32.1*	-30.8*	-31.6*	<0.001
LDL-C	-42.7*	-41.3*	-42.1*	<0.001
HDL-C	+5.1	+4.6	+5.3	>0.05
TG	-28.9*	-27.6*	-28.4*	<0.001
p-value < 0.0001 (highly significant)				

Table 2 summarizes the changes in lipid profile parameters from baseline to 12 weeks within each group. All three regimens resulted in significant reductions in total cholesterol, LDL-C,

and triglycerides ($p < 0.001$). HDL-C showed a modest rise in all groups, but the increase was not statistically significant.

Table 3. Intergroup comparison of mean % change in lipid profile (baseline to 12 weeks)

Parameter	A vs B (p)	A vs C (p)	B vs C (p)
TC	0.71	0.83	0.79
LDL-C	0.66	0.92	0.81
HDL-C	0.84	0.72	0.77
TG	0.69	0.88	0.74

Table 3 compares the percentage changes in lipid parameters between the three treatment groups. No statistically significant differences were observed among the groups, indicating that alternate-day dosing regimens were as effective as daily dosing.

Table 4. Glycemic parameters (baseline vs 12 weeks)

Parameter	Group A	Group B	Group C	p (within)
HbA1c (%)	+0.4*	+0.3*	+0.4*	<0.001
FBS (mg/dL)	+2.6	+2.1	+2.4	>0.05

Table 4 presents the changes in glycemic parameters. A statistically significant increase in HbA1c was observed in all groups, though the absolute rise was modest. FBS increased slightly, but the change was not statistically significant, suggesting no clinically relevant worsening of glycemic control.

Table 5. Adverse events during 12 weeks

Adverse Event	Group A (%)	Group B (%)	Group C (%)
Headache	10.0	6.7	6.7
Myalgia	13.3	6.7	6.7
GI upset	6.7	3.3	3.3
No AE	70.0	83.3	83.3

Table 5 outlines the adverse events reported during the 12-week treatment. Myalgia and headache were the most commonly reported adverse events, occurring more frequently in the daily dosing group. Most events were mild and did not require treatment discontinuation. The majority of participants in the alternate-day groups reported no adverse events.

Discussion

This randomized, open-label, parallel-group trial demonstrated that alternate-day dosing of rosuvastatin, either 10 mg or 20 mg, was comparable to daily 10 mg dosing in terms of lipid-lowering efficacy in patients with dyslipidemia. The three treatment groups were well-matched at baseline for demographic and clinical characteristics, ensuring that the subsequent differences observed were attributable to the interventions.

Over 12 weeks, all regimens significantly reduced total cholesterol, LDL-C, and triglycerides, with the magnitude of LDL-C reduction approaching 42% across groups. These findings are consistent with international evidence, including the

JUPITER trial and smaller studies, which have shown a potent reduction in LDL-C with rosuvastatin [8]. Notably, the absence of statistically significant differences between groups suggests that alternate-day therapy is not inferior to daily dosing. The modest increase in HDL-C across all regimens, though not statistically significant, aligns with the known pharmacological profile of rosuvastatin, which has a greater effect on LDL-C and triglycerides than on HDL-C [9].

A small but statistically significant rise in HbA1c was observed in all groups, while fasting blood glucose increased only slightly and without statistical significance. Although these results echo previous reports linking statins to modest glycemic changes, the absolute alterations were minor and unlikely to have a short-term clinical impact [10-12]. Nevertheless, as statin therapy is long-term, monitoring glycemic status remains advisable, especially in patients with pre-existing risk for diabetes [11].

Adverse events were generally mild and included myalgia, headache, and gastrointestinal upset. These occurred more frequently in the daily dosing group, whereas the majority of participants in the alternate-day groups reported no adverse events [13]. The reduced frequency of side effects with alternate-day dosing is consistent with prior studies and may improve patient adherence to therapy [14-15]. No serious adverse events or treatment discontinuations occurred during the study, supporting the overall safety of rosuvastatin in all regimens tested.

Conclusion

This prospective, randomized, open-label study demonstrated that alternate-day dosing of rosuvastatin (10 mg or 20 mg) is as effective as daily 10 mg dosing in improving lipid profiles among patients with dyslipidemia. All regimens significantly reduced total cholesterol, LDL-C, and triglycerides, while HDL-C showed a modest, non-significant increase. Glycemic parameters exhibited minor changes, with only a slight rise in HbA1c, which is unlikely to be clinically meaningful in the short term. Adverse events were mild and less frequent with alternate-day dosing, suggesting better tolerability and adherence potential. In addition to comparable efficacy, the cost advantage and improved tolerability make alternate-day rosuvastatin a pragmatic and safe therapeutic option for long-term dyslipidemia management in Indian patients. Further multicentric studies with longer follow-up are warranted to confirm these findings and evaluate cardiovascular outcome benefits.

Source of funding: Nil
Conflict of Interest: None
Acknowledgement: None

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Cite this Article: Rani P, raj S. Comparative Efficacy and Safety of Daily Versus Alternate Day Dosing of Rosuvastatin in Dyslipidemic Patients: A Prospective, Randomized, Open Label Study International Journal of Public research in Medicine and Health. July-September 2025; 1(1):10-18. https://doi.org/10.66328/ijprmh.2025.010103