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ARTICLE

Clinical Efficacy of Ezetimibe Combined with Rosuvastatin in the Treatment of Patients with Primary Hypercholesterolemia Inadequately Controlled by Statin Therapy

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Abstract

Aims/Background Primary hypercholesterolemia (PHC) is a major risk factor for atherosclerotic cardiovascular disease (ASCVD). Although the fact that statins effectively lower low-density lipoprotein cholesterol (LDL-C) levels, some patients fail to achieve target LDL-C levels and continue to have a high risk of cardiovascular disease. This study aims to evaluate the clinical efficacy and safety of ezetimibe combined with rosuvastatin in patients with PHC.

Methods This study retrospectively examined 101 patients with PHC who received statins at the cardiology department of Jilin Province FAW General Hospital, between 2021 and 2024. Patients were divided into the observation (ezetimibe combined with rosuvastatin, n = 45) and control (rosuvastatin, n = 66) groups in accordance with their treatment regimens. Data were sourced from the hospital's electronic health records system, and statistical analysis was performed by using SPSS 25.0 software (IBM Corporation, Armonk, NY, USA).

Results Baseline characteristics were similar between the two groups. After 12 weeks of treatment, the reduction in LDL-C levels in the observation group (–0.373 [–0.427, –0.348]) was greater than that in the control group (–0.240 [–0.318, –0.222], $p < 0.001$). The percentage changes in total cholesterol (TC), triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C) levels were significantly better in the observation group (TC: –0.230 [–0.302, –0.144], TG: –0.292 [–0.333, –0.237], and HDL-C: 0.081 [0.067, 0.111]) than in the control group (TC: –0.127 [–0.158, –0.119], TG: –0.082 [–0.101, –0.067], and HDL-C: 0.000 [–0.163, 0.133] with $p < 0.001$, $p < 0.001$, and $p = 0.011$, respectively). Regarding drug safety, the incidence of adverse events was comparable between the two groups (11.10% vs. 12.10%, $p = 0.871$).

Conclusion The combination of ezetimibe and rosuvastatin demonstrates superior lipid-lowering efficacy and good safety in patients with PHC inadequately controlled by statin therapy, providing an effective alternative treatment option. Further large-scale, multicenter randomized controlled trials are warranted to confirm its long-term efficacy and safety.

Key words: ezetimibe; rosuvastatin; primary hypercholesterolemia; low-density lipoprotein cholesterol; clinical efficacy

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Introduction

Primary hypercholesterolemia (PHC) is a major risk factor for atherosclerotic cardiovascular disease (ASCVD) (Saeed et al, 2023). ASCVD, which includes

coronary heart disease, stroke, and peripheral arterial disease, is a major contributor to death and disability worldwide, affecting over 387.85 million people globally in 2019 (Li et al, 2024; Zibaeenejad et al, 2022). Clinically, managing low-density lipoprotein cholesterol (LDL-C) is essential for preventing and treating ASCVD (Wilkinson et al, 2023). Statins are routinely used as the first-line treatment to achieve this goal by inhibiting hepatic cholesterol synthesis, thereby reducing plasma LDL-C levels (Ferri et al, 2024).

Despite the remarkable efficacy of statins in reducing LDL-C levels and cardiovascular events, a considerable number of patients do not achieve the target LDL-C levels recommended by clinical guidelines with statin monotherapy (Krähenbühl et al, 2016). These patients remain at high cardiovascular risk and need alternative treatments with improved efficacy. Additionally, the prolonged use of high-dose statins may lead to side effects, such as myalgia and liver function abnormalities, limiting their use in some patients (Averbukh et al, 2022; Miernik et al, 2024; Saha and Garg, 2021). Therefore, clinical interest in combination therapies to enhance efficacy and reduce side effects is growing.

Ezetimibe is a cholesterol absorption inhibitor that substantially lowers plasma cholesterol levels by inhibiting intestinal cholesterol absorption (Lamb, 2020). The combination of ezetimibe with statins has been shown to reduce LDL-C levels remarkably, demonstrating superior efficacy compared with statin monotherapy in several clinical trials (Chilbert et al, 2022). However, systematic retrospective studies on the specific benefits and safety of combining ezetimibe with rosuvastatin in PHC inadequately controlled by statin therapy are lacking.

The objective of this research is to assess the clinical benefits and safety of ezetimibe combined with rosuvastatin in treating patients with PHC that is inadequately controlled with statin therapy. By retrospectively analyzing patients' clinical data, we hypothesize that combination therapy substantially reduces LDL-C levels while maintaining good tolerability and safety. The necessity of this study lies in the urgent need for effective and safe treatment options for patients with PHC that are inadequately controlled by statin therapy. The combined use of ezetimibe and rosuvastatin is expected to offer a viable treatment alternative, improving patient outcomes.

Methods

Study Design

This study is a retrospective cohort study aiming to evaluate the clinical efficacy and safety of combining ezetimibe with rosuvastatin in patients with PHC that is inadequately controlled with statin therapy. Clinical data were retrospectively reviewed to analyze changes in LDL-C levels and cardiovascular event incidence under different treatment regimens.

Study Population

This study was conducted at the department of cardiology at Jilin Province FAW General Hospital. The study population consisted of patients with PHC who

were treated with statins and visited the hospital between 2021 and 2024. Patients were divided into two groups on the basis of their treatment regimen: the observation (ezetimibe combined with rosuvastatin) and control (rosuvastatin alone) groups. Patients in the observation group received a combination therapy of ezetimibe (10 mg/day) and rosuvastatin (10 mg/day) administered once daily. Patients in the control group were treated with rosuvastatin (10 mg/day) alone, also administered once daily. The statin used was consistent between the two groups. In clinical practice, all patients receive routine dietary education and guidance.

Inclusion Criteria

Patients were included if they were adults aged 18–75 years; diagnosed with primary hypercholesterolemia in accordance with the diagnostic criteria defined by the guidelines of the European Society of Cardiology/European Atherosclerosis Society (Mach et al, 2020); received statin therapy for at least 12 weeks but their LDL-C levels remained above target; treated with ezetimibe combined with rosuvastatin or rosuvastatin alone for at least 12 weeks; and had complete follow-up records during the study period, including biochemical indicators before treatment, at various stages during therapy, and at the conclusion of follow-up.

Exclusion Criteria

Patients were excluded if they had severe liver or renal dysfunction (alanine aminotransferase (ALT) or aspartate aminotransferase (AST) more than twice the upper limit of normal or estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2); had a history of myocardial infarction, stroke, or other severe cardiovascular events; had a known allergy to statins or ezetimibe; had malignancies, active infections, autoimmune diseases, or other severe diseases that might affect study outcomes; were pregnant or lactating; did not adhere to the treatment or follow-up schedule; and had poor medication compliance.

Data Source

Data were sourced from the electronic health record system of the hospital. They included patients' basic information, laboratory test results, treatment regimens, and follow-up records. Collected data were anonymized to protect patient privacy.

Data Collection

Data collection was independently performed by two trained researchers who screened the hospital's electronic health record system for patients meeting the above inclusion and exclusion criteria. The selected patients' treatment and follow-up records during the study period were further verified to ensure the completeness and accuracy of the data. The use of strict inclusion and exclusion criteria and the process of selection aimed to ensure the homogeneity of the study subjects, thus reducing selection bias and enhancing the reliability and generalizability of the study results.

Study Indicators

Baseline Indicators

Demographic Characteristics: Age, gender, height, weight, body mass index (BMI), smoking history, and alcohol consumption history.

Medical History: History of hypertension, diabetes, coronary heart disease, and stroke.

Lipid Indicators: LDL-C, total cholesterol (TC), HDL-C, and triglycerides (TGs).

Liver Function Indicators: ALT, AST, total protein, and albumin.

Renal Function Indicators: Serum creatinine and eGFR.

Study Variables

Lipid Indicators: LDL-C, TC, HDL-C, and TG levels during treatment (at 12 weeks of treatment).

Adverse Reactions: Adverse reactions occurring during and within 12 weeks of treatment with ezetimibe and rosuvastatin (such as myalgia, liver dysfunction, and renal dysfunction).

Data Analysis

Data analysis was performed by using Statistical Product and Service Solutions (SPSS) 25.0 software (IBM Corporation, Armonk, NY, USA). First, descriptive statistical analysis was conducted on the baseline characteristics of the observation and control groups. Continuous variables were assessed for normality by using the Shapiro–Wilk test. Variables that followed a normal distribution were expressed as mean ± standard deviation, whereas those that did not meet the normality assumption were described by using median and interquartile range (IQR). Group comparisons for continuous variables with a normal distribution were performed by applying independent samples *t*-tests. For variables that did not follow a normal distribution, nonparametric tests, such as the Mann–Whitney U test, were employed. Categorical variables were expressed in the form of percentages, and comparisons between groups were performed by employing the chi-square test. Subsequently, changes in primary efficacy indicators (such as LDL-C, TC, HDL-C, and TG) were assessed in the observation and control groups by comparing measurements taken prior to and following the treatment. Percent changes in measurements were calculated to assess baseline changes and differences between groups as percent change = (12 weeks of treatment – before treatment)/before treatment. Multiple linear regression analysis was conducted to explore the factors influencing the percentage change in LDL-C. Herein, $p < 0.05$ was considered statistically significant.

Results

Baseline Characteristics

This study comprised 101 participants, with 45 participants in the observation group receiving a combination of ezetimibe and rosuvastatin and 66 individuals in the treatment group treated exclusively with rosuvastatin. No significant differ-

ences were found between the two groups in terms of age, gender, BMI, smoking history, alcohol consumption history, hypertension history, diabetes, coronary heart disease, stroke, medication history (statins, fibrates, and niacin), ALT, AST, total protein, albumin, serum creatinine, and eGFR. Detailed baseline characteristics are provided in Table 1. The similarity in baseline characteristics between the observation and control groups provided a solid foundation for comparing the efficacy and safety of the treatments.

Table 1. General demographic indicators of the two groups ($\bar{\chi} \pm s$, n [%]).

Characteristic	Observation group (n = 45)	Control group (n = 66)	t/χ^2	p
Demographics				
Age (years)	60.34 ± 8.21	58.97 ± 7.56	0.905	0.367
Gender			0.000	0.991
Male	28 (62.2%)	41 (62.1%)		
Female	17 (37.8%)	25 (37.9%)		
BMI (kg/m^2)	24.53 ± 3.14	24.86 ± 2.95	0.564	0.574
Smoking history			0.069	0.793
Positive	14 (31.1%)	19 (28.8%)		
Negative	31 (68.9%)	47 (71.2%)		
Alcohol history			0.065	0.799
Positive	18 (40.0%)	28 (42.4%)		
Negative	27 (60.0%)	38 (57.6%)		
Medical history				
Hypertension			0.035	0.852
Yes	32 (71.1%)	48 (72.7%)		
No	13 (28.9%)	18 (27.3%)		
Diabetes			0.044	0.833
Yes	20 (44.4%)	28 (42.4%)		
No	25 (55.6%)	38 (57.6%)		
Coronary heart disease			0.051	0.822
Yes	18 (40.0%)	25 (37.9%)		
No	27 (60.0%)	41 (62.1%)		
Stroke history			0.004	0.950
Yes	10 (22.2%)	15 (22.7%)		
No	35 (77.8%)	51 (77.3%)		
Baseline biochemical parameters				
ALT (U/L)	26.53 ± 5.22	27.83 ± 6.15	1.161	0.248
AST (U/L)	24.36 ± 4.81	23.98 ± 5.23	0.388	0.699
Total protein (g/L)	70.23 ± 5.64	69.89 ± 5.41	0.320	0.750
Albumin (g/L)	42.52 ± 3.24	42.88 ± 3.18	0.581	0.562
Serum creatinine (μmol/L)	85.49 ± 12.32	83.94 ± 11.85	0.666	0.507
eGFR (mL/min/1.73 m^2)	87.37 ± 9.88	88.18 ± 10.22	0.416	0.679

Note: BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; eGFR, estimated glomerular filtration rate.

Table 2. Changes in LDL-C levels in the two groups ($\bar{\chi} \pm$ s/M [IQR]).

Time point	Observation group (n = 45)	Control group (n = 66)	z	*p*
Before treatment (mmol/L)	4.80 ± 0.70	4.69 ± 0.80	-	-
After treatment (mmol/L)	2.90 ± 0.50	3.50 ± 0.60	-	-
Percentage change	−0.373 (−0.427, −0.348)	−0.240 (−0.318, −0.222)	−6.963	<0.001

Note: LDL-C, low-density lipoprotein cholesterol; M, median; IQR, interquartile range.

Table 3. Other lipid changes in both groups ($\bar{\chi} \pm$ s/M [IQR]).

Indicators	Time point	Observation group (n = 45)	Control group (n = 66)	z	*p*
TC (mmol/L)	Before treatment	6.15 ± 0.90	6.00 ± 0.80		
	After treatment	4.81 ± 0.68	5.20 ± 0.60		
	Percentage change	−0.230 (−0.302, −0.144)	−0.127 (−0.158, −0.119)	−3.965	<0.001
HDL-C (mmol/L)	Before treatment	1.20 ± 0.30	1.30 ± 0.40	-	-
	After treatment	1.30 ± 0.30	1.31 ± 0.34	-	-
	Percentage change	0.081 (0.067, 0.111)	0.000 (−0.163, 0.133)	−2.528	0.011
TG (mmol/L)	Before treatment	2.50 ± 0.60	2.42 ± 0.66	-	-
	After treatment	1.80 ± 0.41	2.20 ± 0.50	-	-
	Percentage change	−0.292 (−0.333, −0.237)	−0.082 (−0.101, −0.067)	−7.136	<0.001

Note: TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; M, median; IQR, interquartile range.

Changes in LDL-C Levels

Table 2 presents the LDL-C level changes observed before and after treatment in each group. Although both groups experienced significant reductions in LDL-C levels after treatment, the reduction was more pronounced in the observation group than in the control group. The percentage change in LDL-C levels after treatment was –0.373 (–0.427, –0.348) in the observation group and –0.240 (–0.318, –0.222) in the control group. The variation in percentage change between groups was statistically significant (z = –6.963, $p < 0.001$).

Changes in Other Lipid Levels

Table 3 shows the changes in TC, HDL-C, and TG levels in both groups. The percentage change in TC levels was notably greater in the observation group (–0.230 [–0.302, –0.144]) than in the control group (–0.127 [–0.158, –0.119]) (z = –3.965, $p < 0.001$). The percentage change in HDL-C levels was significantly greater in the observation group (0.081 [0.067, 0.111]) than in the control group (0.000 [–0.163, 0.133]) (z = –2.528, $p = 0.011$). The percentage change in TG levels was markedly greater in the observation group (0.292 [–0.333, –0.237]) than in the control group (–0.082 [–0.101, –0.067]) (z = –7.136, $p < 0.001$).

Multivariate Regression Analysis of LDL-C Percentage Change

Linear regression analysis was conducted with baseline characteristics included in the regression model and LDL-C percentage change as the dependent variable.

Table 4. Multivariate regression analysis of LDL-C percentage change.

Characteristic	B	SE	β	t	p
Treatment regimen	−0.144	0.017	−0.639	−8.629	<0.001
Age	−0.001	0.001	−0.047	−0.643	0.522
BMI	−0.004	0.003	−0.112	−1.325	0.188
Gender	−0.022	0.018	−0.097	−1.258	0.212
Smoking history	−0.001	0.018	−0.005	−0.068	0.946
Alcohol history	0.012	0.016	0.056	0.777	0.439
Hypertension	0.005	0.018	0.021	0.287	0.775
Diabetes	0.009	0.016	0.040	0.568	0.572
Coronary heart disease	−0.014	0.017	−0.060	−0.822	0.413
Stroke history	0.013	0.018	0.054	0.720	0.473
ALT	−0.004	0.002	−0.232	−1.928	0.057
AST	−0.001	0.002	−0.066	−0.810	0.420
Total protein	0.004	0.002	0.190	1.615	0.110
Albumin	0.003	0.003	0.079	0.866	0.389
Serum creatinine	−0.001	0.001	−0.147	−0.996	0.322
eGFR	−0.002	0.002	−0.139	−0.966	0.336

Note: R^2 = 0.563, adjusted R^2 = 0.489, F = 7.573, $p < 0.001$; BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; eGFR, estimated glomerular filtration rate; SE, Standard Error.

In the regression model, the treatment regimen was the only significant predictor (β = –0.639, $p < 0.001$), indicating it had the most substantial effect on LDL-C percentage change. The model explained 48.9% of the variance. These results, detailed in Table 4, enhance the reliability of the study's conclusions.

Drug Safety

No notable disparity in adverse event rates was observed between the observation and control groups during the treatment period. The incidence of adverse events was 11.10% (5/45) in the observation group and 12.10% (8/66) in the control group (χ^2 = 0.026, p = 0.871). The details of the specific adverse events are shown in Fig. 1.

Discussion

This study sought to assess the clinical effectiveness and safety of combining ezetimibe with rosuvastatin in patients with PHC that did not achieve adequate control with statins alone. The results demonstrated that the ezetimibe plus rosuvastatin treatment significantly reduced the levels of LDL-C, TC, and TG compared with rosuvastatin alone. This finding indicates that cholesterol absorption inhibition by ezetimibe combined with cholesterol synthesis inhibition by rosuvastatin effectively improves lipid control in patients. Controlling LDL-C levels is a critical clinical strategy for preventing and managing ASCVD. For patients inadequately treated with statins, the ezetimibe and rosuvastatin combination therapy offers an

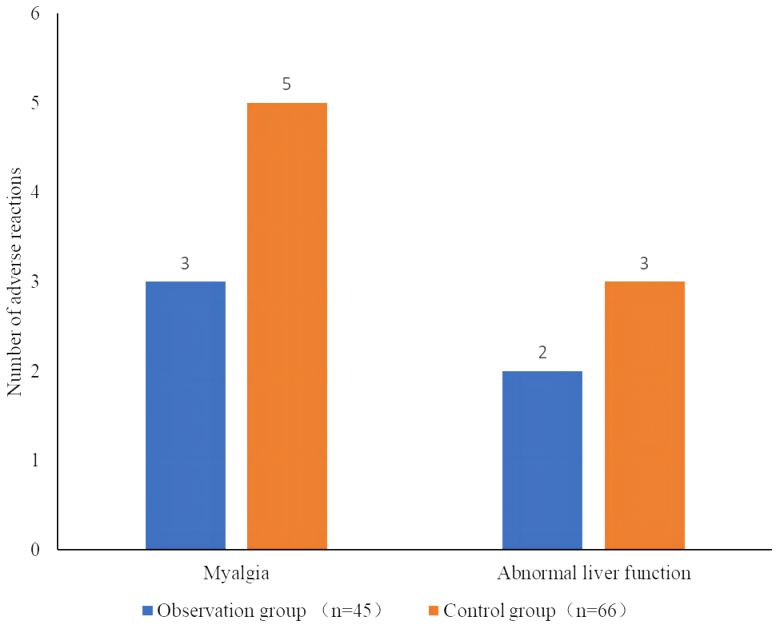

Fig. 1. Details of adverse events.

effective alternative treatment option, potentially reducing cardiovascular events and enhancing long-term outcomes.

Hong et al (2018) conducted a randomized controlled trial over 8 weeks at 20 hospitals in Korea. Their trial revealed that combining ezetimibe with rosuvastatin notably enhanced lipid profiles in patients with hypercholesterolemia compared with using rosuvastatin alone. Patients taking rosuvastatin with ezetimibe experienced an average LDL-C reduction of more than 50%. This study indicates that ezetimibe, as a cholesterol absorption inhibitor, when used in combination with statins, provides an effective treatment option for patients with PHC. Our findings are consistent with the above results while further validating the efficacy of combination therapy across various clinical contexts and patient populations. Lee et al (2021) performed a multicenter, randomized, double-blind trial to assess if low-dose rosuvastatin combined with ezetimibe could serve as a viable substitute for moderate-dose rosuvastatin alone in patients needing cholesterol reduction. Their results indicated that the low-dose rosuvastatin and ezetimibe combination was more effective in reducing LDL cholesterol and reaching target levels than moderate-dose rosuvastatin alone. Similarly, Rhee et al (2019) demonstrated that the lipid-lowering effects of ezetimibe combined with low or moderate intensity statin therapy were comparable or superior to those of high-intensity rosuvastatin monotherapy. The advantage of ezetimibe combination therapy lies in its ability to reduce the dose of rosuvastatin without compromising its lipid-lowering efficacy. These studies conducted follow-ups for 8 weeks, whereas our study collected data at 12 weeks posttreatment to further explore the long-term efficacy of combination therapy in real-world clinical settings. Choi et al (2023) showed that for patients with ASCVD, moderate-intensity rosuvastatin combined with ezetimibe had superior LDL-C-lowering efficacy over high-intensity rosuvastatin monotherapy without increasing adverse reactions. Consistent with previous safety findings, our study results

did not illustrate significant differences in the incidence of adverse events between the treatment and control groups during drug therapy, indicating that ezetimibe combined with rosuvastatin therapy has an acceptable risk profile. Through practical clinical implementation, this study further confirms the feasibility and safety of this approach in real clinical environments, representing a crucial step in translating research findings into clinical practice. Our study is related to the work of Su et al (2023), which evaluated the efficacy and safety of the combination of rosuvastatin and 10 mg/ezetimibe in Chinese patients. This study utilized a randomized, double-blind, double-dummy, active-controlled phase 3 clinical trial design and demonstrated that the combination significantly reduced LDL-C levels within 8 weeks. Our research presents several innovations. First, we utilized real-world data through a retrospective cohort analysis and electronic health records, providing insights into the effectiveness of the combination of ezetimibe and rosuvastatin in actual clinical settings, thereby enhancing the applicability of the results. Second, our study included a 12-week follow-up, exploring the long-term effects of the combination therapy, whereas Su et al (2023)'s study focused primarily on short-term effects over 8 weeks. Our long follow-up offers additional data on the sustained efficacy of the combination therapy, further complementing existing research and providing valuable evidence for practical application.

The effectiveness of ezetimibe combined with rosuvastatin in treating primary hypercholesterolemia has been confirmed in numerous studies (Barrios and Escobar, 2021; Farnier et al, 2016; Kang et al, 2024; Vattimo et al, 2020). Our study conducted a retrospective analysis using real-world clinical data, providing evidence complementing the findings of randomized controlled trials. It encompassed patient populations with diverse clinical backgrounds and characteristics, thereby enhancing the generalizability and practical applicability of its results. Our study's long follow-up duration yielded valuable data on long-term efficacy and safety.

Despite achieving some remarkable results, our study has several limitations that need consideration. First, it is a single-center retrospective study, which may introduce selection bias and information bias. Its single-center design limits the generalizability of its findings because its sample may not be representative of patients from other institutions. Being a retrospective study, it relies on existing medical records, which may be affected by inaccuracies and incomplete data. Additionally, patients with missing data were excluded, potentially introducing discrepancies. We implemented stringent inclusion criteria and data screening to address the above limitations. Future research should consider a multicenter approach to improve generalizability and a prospective design to reduce biases. Standardizing data collection and recording procedures will further enhance data accuracy and reliability. Second, our sample size, though statistically adequate, limits the generalizability of our study's findings. Additionally, we did not comprehensively record and assess all potential influencing factors, such as lifestyle interventions and other medication use, which could affect the study results. Future research should include detailed information on concomitant medication use, particularly among diabetic patients, to address potential confounding factors. Such information includes medications, including insulin and oral hypoglycemic agents (e.g., GLP-1 recep-

tor agonists and SGLT2 inhibitors). Furthermore, no notable differences in safety were found between groups, and the further verification of the long-term safety of the ezetimibe–rosuvastatin combination through long-term follow-up studies with large sample sizes is warranted. Moreover, increasing the sample size and exploring treatment responses in different dosage subgroups should be considered in future research. Also, a key limitation of this study is the absence of a placebo control group. This deficiency makes fully evaluating the efficacy of the combination therapy without accounting for potential placebo effects difficult. Placebo-controlled trials are essential to differentiate between actual treatment effects and psychological responses. Future research should include a placebo group to clarify the true efficacy of the drug combination and ensure that the observed benefits are due to the treatment rather than patient expectations or other nonspecific factors. Finally, although all patients typically receive routine dietary education and guidance in clinical practice to help manage cholesterol levels, this study, being retrospective in nature, did not include direct dietary interventions during the treatment period. We were unable to control for dietary factors throughout the study, which could potentially influence cholesterol levels. However, given that all patients were under standard clinical management with dietary guidance, we believe that this limitation has minimal impact on the main conclusions of the study. Nonetheless, future prospective studies should explore the specific effects of standardized dietary education on cholesterol management to provide more comprehensive evidence.

Conclusion

The combination therapy of ezetimibe with rosuvastatin demonstrates favorable clinical efficacy in patients with suboptimal statin treatment effects for PHC. It remarkably lowers LDL-C levels and improves other lipid profiles while maintaining good safety and tolerability. This combined treatment strategy holds promise as a new therapeutic option for managing hypercholesterolemia in clinical practice. However, further large-scale, multicenter randomized controlled trials are needed to validate its long-term efficacy and safety.

Key Points

- In patients with PHC inadequately managed by statin therapy, ezetimibe combined with rosuvastatin substantially enhances lipid control compared with rosuvastatin alone.
- The combination therapy leads to great reductions in LDL-C, TC, and TG and an increase in HDL-C levels, demonstrating superior efficacy.
- The combination and monotherapy groups have similar drug safety profiles without significant differences in adverse event rates.
- The approach reported in this article provides an effective alternative for managing hypercholesterolemia. However, further large-scale studies are needed to confirm its long-term benefits and safety.

Availability of Data and Materials

Data and materials from this study can be obtained from the corresponding author upon reasonable request.

Author Contributions

The study was designed by ZW and FW, and ZW, FW and WD were involved in its execution. ZW and LZ handled data collection and analysis. ZW and WD contributed to drafting the manuscript, and all authors engaged in the critical revision of the manuscript. All authors approved the final manuscript and took responsibility for the integrity of the work, ensuring that any concerns about accuracy or completeness are addressed.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Jilin Province FAW General Hospital (K2023-003-01). All patients provided informed consent before data collection. The study strictly adhered to the Declaration of Helsinki and relevant ethical standards to ensure patient rights and privacy protection.

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Conflict of Interest

The authors declare no conflict of interest.

References

Averbukh LD, Turshudzhyan A, Wu DC, Wu GY. Statin-induced Liver Injury Patterns: A Clinical Review. Journal of Clinical and Translational Hepatology. 2022; 10: 543–552. https://doi.org/10.14218/JCTH.2021.00271

Barrios V, Escobar C. Fixed-dose combination of rosuvastatin and ezetimibe: treating hypercholesteremia according to cardiovascular risk. Expert Review of Clinical Pharmacology. 2021; 14: 793–806. https://doi.org/10.1080/17512433.2021.1925539

Chilbert MR, VanDuyn D, Salah S, Clark CM, Ma Q. Combination Therapy of Ezetimibe and Rosuvastatin for Dyslipidemia: Current Insights. Drug Design, Development and Therapy. 2022; 16: 2177–2186. https://doi.org/10.2147/DDDT.S332352

Choi H, Kang SH, Jeong SW, Yoon CH, Youn TJ, Song WH, et al. Lipid-Lowering Efficacy of Combination Therapy With Moderate-Intensity Statin and Ezetimibe Versus High-Intensity Statin Monotherapy: A Randomized, Open-Label, Non-Inferiority Trial From Korea. Journal of Lipid and Atherosclerosis. 2023; 12: 277–289. https://doi.org/10.12997/jla.2023.12.3.277

Farnier M, Jones P, Severance R, Averna M, Steinhagen-Thiessen E, Colhoun HM, et al. Efficacy and safety of adding alirocumab to rosuvastatin versus adding ezetimibe or doubling the rosuvastatin dose in high cardiovascular-risk patients: The ODYSSEY OPTIONS II randomized trial. Atherosclerosis. 2016; 244: 138–146. https://doi.org/10.1016/j.atherosclerosis.2015.11.010

Ferri N, Ruscica M, Fazio S, Corsini A. Low-Density Lipoprotein Cholesterol-Lowering Drugs: A Narrative Review. Journal of Clinical Medicine. 2024; 13: 943. https://doi.org/10.3390/jcm13040943

Hong SJ, Jeong HS, Ahn JC, Cha DH, Won KH, Kim W, et al. A Phase III, Multicenter, Randomized, Double-blind, Active Comparator Clinical Trial to Compare the Efficacy and Safety of Combination Therapy With Ezetimibe and Rosuvastatin Versus Rosuvastatin Monotherapy in Patients With Hypercholesterolemia: I-ROSETTE (Ildong Rosuvastatin & Ezetimibe for Hypercholesterolemia) Randomized Controlled Trial. Clinical Therapeutics. 2018; 40: 226–241.e4. https://doi.org/10.1016/j.clinthera.2017.12.018

Kang Y, Park JM, Lee SH. Moderate-Intensity Rosuvastatin/Ezetimibe Combination versus Quadruple-Dose Rosuvastatin Monotherapy: A Meta-Analysis and Systemic Review. Yonsei Medical Journal. 2024; 65: 19–26. https://doi.org/10.3349/ymj.2023.0285

Krähenbühl S, Pavik-Mezzour I, von Eckardstein A. Unmet Needs in LDL-C Lowering: When Statins Won't Do! Drugs. 2016; 76: 1175–1190. https://doi.org/10.1007/s40265-016-0613-0

Lamb YN. Rosuvastatin/Ezetimibe: A Review in Hypercholesterolemia. American Journal of Cardiovascular Drugs: Drugs, Devices, and other Interventions. 2020; 20: 381–392. https://doi.org/10.1007/s40256-020-00421-1

Lee SA, Kim W, Hong TJ, Ahn Y, Kim MH, Hong SJ, et al. Effects of Fixed-dose Combination of Low-intensity Rosuvastatin and Ezetimibe Versus Moderate-intensity Rosuvastatin Monotherapy on Lipid Profiles in Patients With Hypercholesterolemia: A Randomized, Double-blind, Multicenter, Phase III Study. Clinical Therapeutics. 2021; 43: 1573–1589. https://doi.org/10.1016/j.clinthera.2021.07.016

Li Z, Yang Y, Wang X, Yang N, He L, Wang J, et al. Comparative analysis of atherosclerotic cardiovascular disease burden between ages 20-54 and over 55 years: insights from the Global Burden of Disease Study 2019. BMC Medicine. 2024; 22: 303. https://doi.org/10.1186/s12916-024-03527-4

Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. European Heart Journal. 2020; 41: 111–188. https://doi.org/10.1093/eurheartj/ehz455

Miernik S, Matusiewicz A, Olesińska M. Drug-Induced Myopathies: A Comprehensive Review and Update. Biomedicines. 2024; 12: 987. https://doi.org/10.3390/biomedicines12050987

Rhee MY, Kim KJ, Kim SH, Yoon YW, Rha SW, Hong SJ, et al. Ezetimibe and Rosuvastatin Combination Treatment Can Reduce the Dose of Rosuvastatin Without Compromising Its Lipid-lowering Efficacy. Clinical Therapeutics. 2019; 41: 2571–2592. https://doi.org/10.1016/j.clinthera.2019.10.010

Saeed AB, Abaalkhail BA, Ismail I, Saeed A, Al-Khammash S. Estimate a patient's 10 years cardiovascular risk using the Arteriosclerotic cardiovascular disease tool in a cross-sectional study in Al-Harja, Asser, Saudi Arabia, 2021. Journal of Family Medicine and Primary Care. 2023; 12: 1106–1112. https://doi.org/10.4103/jfmpc.jfmpc_2183_22

Saha A, Garg A. Severe Liver Injury Associated With High-Dose Atorvastatin Therapy. Journal of Investigative Medicine High Impact Case Reports. 2021; 9: 23247096211014050. https://doi.org/10.1177/23247096211014050

Su Q, Liu Y, Zhang G, Xu L, Wang M, Mei S, et al. Efficacy and Safety of Single-Pill Combination of Rosuvastatin and Ezetimibe in Chinese Patients with Primary Hypercholesterolemia Inadequately Controlled by Statin Treatment (ROZEL): A Randomized, Double-Blind, Double Dummy, Active-Controlled Phase 3 Clinical Trial. Advances in Therapy. 2023; 40: 5285–5299. https://doi.org/10.1007/s12325-023-02666-z

Vattimo ACA, Fonseca FAH, Morais DC, Generoso LF, Herrera R, Barbosa CM, et al. Efficacy and Tolerability of a Fixed-Dose Combination of Rosuvastatin and Ezetimibe Compared with a Fixed-Dose Combination of Simvastatin and Ezetimibe in Brazilian Patients with Primary Hypercholesterolemia or Mixed Dyslipidemia: A Multicenter, Randomized Trial. Current Therapeutic Research, Clinical and Experimental. 2020; 93: 100595. https://doi.org/10.1016/j.curtheres.2020.100595

Wilkinson MJ, Lepor NE, Michos ED. Evolving Management of Low-Density Lipoprotein Cholesterol: A Personalized Approach to Preventing Atherosclerotic Cardiovascular Disease

Across the Risk Continuum. Journal of the American Heart Association. 2023; 12: e028892. https://doi.org/10.1161/JAHA.122.028892

Zibaeenejad F, Mohammadi SS, Sayadi M, Safari F, Zibaeenezhad MJ. Ten-year atherosclerosis cardiovascular disease (ASCVD) risk score and its components among an Iranian population: a cohort-based cross-sectional study. BMC Cardiovascular Disorders. 2022; 22: 162. https://doi.org/10.1186/s12872-022-02601-0