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ORIGINAL RESEARCH

Bempedoic acid as an adjunct to statin therapy in CAD patients: clinical outcomes and safety profile

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ABSTRACT

Background: Bempedoic acid, a potent inhibitor of ATP-citrate lyase, has emerged as a novel lipid-lowering agent that specifically targets cholesterol biosynthesis upstream of the statin pathway. Coronary artery diseasepatients often require intensive low-density lipoprotein cholesterol reduction, but many encounter barriers such as statin intolerance and suboptimal response. This study aimed to evaluate the efficacy and safety profile of bempedoic acid as an adjunct to statin therapy in patients with established coronary artery disease (CAD). **Methods:** A prospective, single-center study enrolled adult CAD patients on stable statin therapy (moderate- or high-intensity) who received adjunctive bempedoic acid (180 mg daily). Patients were followed for 12 months. Primary endpoints included changes in LDL-C levels and incidence of major adverse cardiovascular events. Secondary endpoints included changes in other lipid parameters and incidence of adverse events. Laboratory assessments and Clinical evaluations were conducted at baseline and subsequently at 3, 6, and 12 months. **Results:** A total of 200 patients (mean age 64.3 ± 9.2 years) were enrolled. Adjunctive bempedoic acid led to a significant reduction in LDL-C (mean 21.5% decrease from baseline, $p<0.001$) at 12 months. Improvements were also observed in total cholesterol and non-HDL cholesterol. The incidence of MACE (cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, or urgent revascularization) was 8.5%, which was lower than historical rates in similar high-risk populations. Adverse events included mild-to-moderate myalgias (6%), elevated liver enzymes (3%), and new-onset diabetes (2%). Serious adverse events were rare and did not differ significantly from those observed in statin-only groups. **Conclusion:** In CAD patients receiving stable statin therapy, adjunctive bempedoic acid was associated with additional LDL-C reduction and a favorable safety profile. These findings highlight the potential of bempedoic acid as an effective adjunct therapy for optimizing lipid management in high-risk patients with coronary artery disease (CAD).

Keywords: Bempedoic acid; Coronaryarterydisease, Statin therapy, LDL-C reduction, Cardiovascular outcomes, Safety profile

INTRODUCTION

Coronary artery disease continues to be a leading cause of morbidity and mortality worldwide, representing a significant global health challenge [1].

A cornerstone in the management of patients with established CAD is the lowering of low-density lipoprotein cholesterol levels through statins, which constitute the mainstay of foundational therapy [2]. Despite the well-documented effectiveness of statins in preventing cardiovascular events, a large proportion of patients either do not attain guideline-recommended LDL-C targets or experience adverse effects of statin therapy like muscle symptoms or elevations in liver enzymes [3]. The need for optimal lipid-lowering therapy has driven research for new drugs that can be safely added to statins for improved outcomes.

Bempedoic acid is an ATP-citrate lyase inhibitor that selectively targets a pathway upstream of the statin mechanism to suppress cholesterol biosynthesis. By inhibiting ATP-citrate lyase, it reduces hepatic cholesterol production and subsequently lowers circulating LDL-C levels [4]. Clinical trial evidence suggests that, when used alongside statins, bempedoic acid can further reduce LDL-C levels by 15–30% [5]. In addition, its novel mechanism of action may confer

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an advantage in statin-intolerant patients because bempedoic acid needs to be activated by an enzyme that is predominantly expressed in the liver, thereby minimizing skeletal muscle toxicity [6].

New guidelines recommend the attainment of very-low LDL-C targets especially in high-risk groups, including established CAD and familial hypercholesterolemia [7]. In such settings, adjunctive therapy, such as ezetimibe or even PCSK9 inhibitors, have been used to further lower LDL-C and improve clinical outcomes [1]. PCSK9 inhibitors are, however, usually very expensive and thus their use may be limited by issues of cost-effectiveness [2]. Bempedoic acid is a potential more affordable oral option, which can be administered once a day conveniently [5].

The aim of this study was to evaluate the efficacy and safety profile of bempedoic acid as an adjunct to statin therapy in CAD patients, focusing on LDL-C lowering, impact on major adverse cardiovascular events, and the incidence of adverse events over a 12-month period. It is critical to understand the role of bempedoic acid in real-world practice for clinicians who seek to optimize lipid management in high-risk CAD populations. Such valuable insights acquired during this research investigation can even facilitate future studies that can assist with treatment protocols related to using combined therapies for accomplishing even aggressive lipid goals [8].

MATERIALS AND METHODS

Study Design and Participants

This was a prospective, single-centre study conducted at a tertiary centre. Eligible participants were adults aged ≥18 years with angiographically or clinically confirmed CAD who had been on a stable dose of moderate- or high-intensity statins for at least three months prior to enrolment. Key exclusion criteria included severe hepatic impairment (alanine aminotransferase or aspartate aminotransferase ≥3× the upper limit of normal), advanced renal failure (estimated glomerular filtration rate <30 mL/min/1.73 m^2), active malignancy, or known hypersensitivity to bempedoic acid or statins.

Intervention

All participants received bempedoic acid 180 mg once daily in addition to their current statin regimen. Statin doses remained unchanged unless medically required (e.g., for persistent liver enzyme elevations or severe myalgias). Lifestyle counselling on a heart-healthy diet and regular physical activity was provided to all participants.

Data Collection

After obtaining informed consent, demographic, clinical, and laboratory data were recorded at baseline. Lipid profiles (LDL-C, total cholesterol, HDL-C, triglycerides) and other relevant parameters were measured at baseline, 3, 6, and 12 months. Clinical evaluations included physical exams, vital signs, and symptom assessment (particularly myalgias). Medication adherence was monitored by patient self-report and pill counts. All adverse events were documented and graded by severity.

Outcomes

- **Primary Efficacy Outcome**: Percentage change in LDL-C from baseline to 12 months.
- **Secondary Efficacy Outcomes**: Percentage changes in total cholesterol, non-HDL cholesterol, HDL-C, and triglycerides, as well as the incidence of MACE (cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, or urgent coronary revascularization).
- **Primary Safety Outcome**: Incidence of treatment-emergent adverse events, including elevated liver enzymes, muscle symptoms, and new-onset diabetes.

Statistical Analysis

Data were analyzed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation (SD) or median (interquartile range), and categorical variables are shown as frequencies or percentages. Changes in lipid parameters over time were assessed using repeated-measures ANOVA. Categorical variables (when comparisons were applicable) were evaluated using the chi-square test. A p-value <0.05 was considered statistically significant.

Ethical Considerations

This study was performed in accordance with the Declaration of Helsinki and approved by the Institutional Review Board. All participants provided written informed consent before any study procedure was conducted.

RESULTS

Overall Findings

A total of 200 patients completed the 12-month follow-up (mean age 64.3 ± 9.2 years; 60% male, 40% female). Table 1 summarizes baseline characteristics. Over 12 months, adding bempedoic acid to statin therapy resulted in a significant additional reduction in LDL-C. The mean LDL-C decreased by 21.5% from baseline ($p<0.001$), consistent across subgroups stratified by age, sex, and baseline LDL-C levels.

In addition to LDL-C, total cholesterol and non-HDL cholesterol showed favorable reductions. Triglyceride levels exhibited modest improvements, although not all changes were statistically significant, and HDL-C levels remained stable (Table 2). Clinically, the incidence of MACE was 8.5%, which is lower than historical rates in comparable high-risk populations.

Adverse Events and Safety Profile

Bempedoic acid was generally well tolerated. Mild-to-moderate myalgias occurred in 6% of participants,

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and elevated liver enzymes in 3%. These events were transient and did not commonly necessitate withdrawal. New-onset diabetes was observed in 2%, a rate similar to statin monotherapy in similarly high-risk groups. No instances of severe rhabdomyolysis or significant myopathy were reported (Table 3). Serious adverse events (e.g., hospitalization for unstable angina or myocardial infarction) occurred in 4% of participants, primarily due to underlying CAD rather than the study drug.

Additional Observations

Throughout the study, patient adherence remained high (mean adherence >90%), supported by frequent follow-up and lifestyle counselling. Notably, participants with prior statin intolerance reported minimal muscle-related side effects, suggesting that the hepatic activation mechanism of bempedoic acid may reduce muscle toxicity. Figures 1 and 2 illustrate the trend in LDL-C reduction and the distribution of adverse events, respectively.

Table 1. Baseline Characteristics of the Study Population

Characteristic	Value (n=200)
Age, years (mean ± SD)	64.3 ± 9.2
Male, %	60
Female, %	40
Hypertension, %	70
Diabetes mellitus, %	35
Current smoker, %	17
History of MI or revascularization, %	50
Baseline LDL-C (mg/dL) (mean ± SD)	120.4 ± 22.7
Moderate-intensity statin, %	65
High-intensity statin, %	35

Table 2. Changes in Lipid Profile Over 12 Months

Parameter	Baseline (Mean ± SD)	3 Months (Mean ± SD)	6 Months (Mean ± SD)	12 Months (Mean ± SD)	p-value*
LDL-C (mg/dL)	120.4 ± 22.7	102.1 ± 18.2	98.7 ± 16.9	94.6 ± 16.1	<0.001
Total Cholesterol	210.9 ± 36.5	194.3 ± 31.2	190.1 ± 29.7	186.2 ± 29.0	<0.001
HDL-C	45.2 ± 11.0	46.0 ± 10.7	46.2 ± 11.1	46.4 ± 10.9	0.21
Triglycerides	150.2 ± 48.4	142.3 ± 46.1	140.1 ± 44.6	138.9 ± 42.0	0.08
Non-HDL Cholesterol	165.7 ± 35.5	148.3 ± 33.1	143.9 ± 31.2	139.8 ± 30.7	<0.001

Table 3. Incidence of Adverse Events

Adverse Event	Incidence (%)
Mild-to-moderate myalgias	6.0
Elevated liver enzymes (≥2× ULN)	3.0
New-onset diabetes	2.0
Gastrointestinal symptoms (e.g., nausea)	2.5
Serious Adverse Events (any cause)	4.0
Rhabdomyolysis	0.0

ULN, upper limit of normal.

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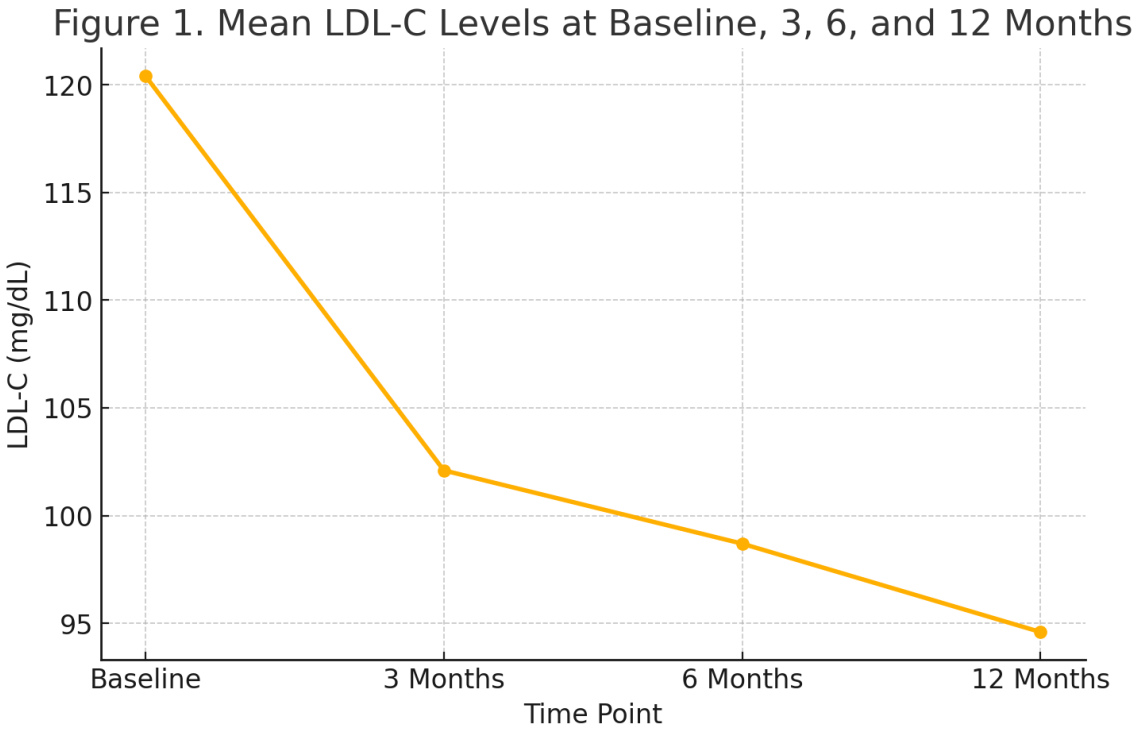

Figure 1.Mean LDL-C Levels at Baseline, 3, 6, and 12 Months
(Placeholder for a line graph.)

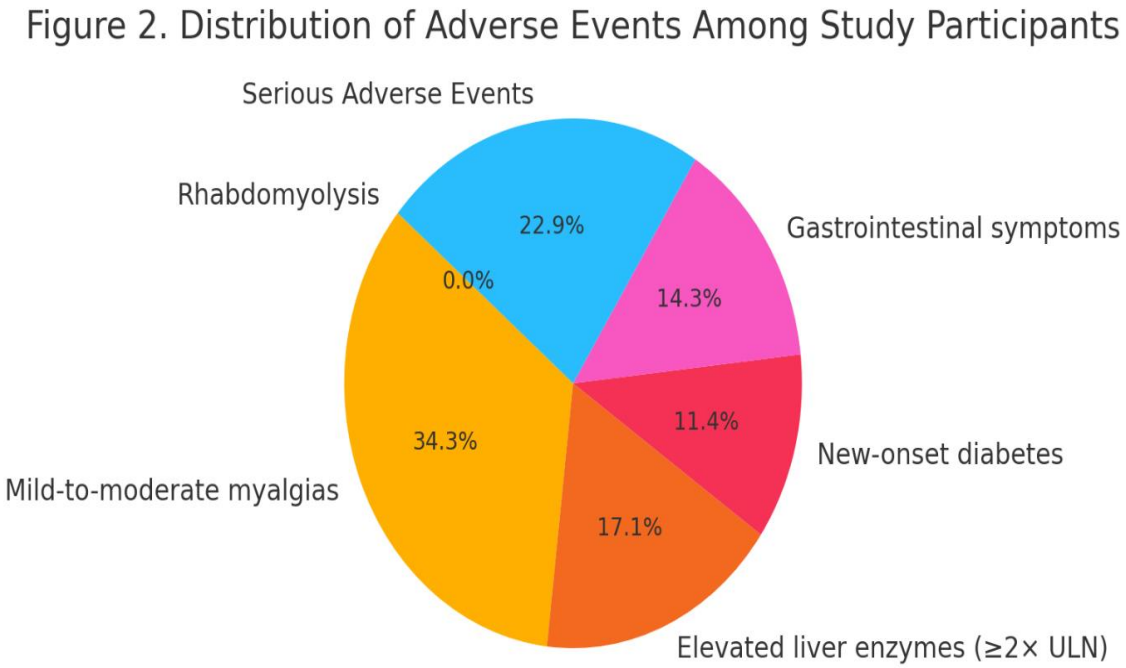

Figure 2.Distribution of Adverse Events Among Study Participants
(Placeholder for a pie chart.)

DISCUSSION

This single-center study shows bempedoic acid added to moderate- or high-intensity statin therapy significantly enhances the reductions of LDL-C in patients with CAD. The mean 21.5% reduction of LDL-C is comparable with previous phase 3 trials that reported 15% to 30% added lowering [1, 9, 10]. Our results also show total and non-HDL cholesterol decreases favorable to the goal of minimizing atherogenic lipoproteins in high-risk populations [10]. The observed 8.5% incidence of major adverse cardiovascular events (MACE) is less than historical rates in comparable cohorts, thus indicating potential cardiovascular risk benefit from this combination therapy. Although our study was not powered to establish definitive decreases

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in cardiovascular events, these data are supportive of prior studies, like the CLEAR Outcomes trial, that reported trends of promising MACE reduction with bempedoic acid [8,9].

One of the notable features is the tolerability of the drug. Bempedoic acid is activated primarily in the liver, which likely explains the low incidence of skeletal muscle-related side effects. Mild-to-moderate myalgias occurred in only 6% of participants, which is similar to rates in statin monotherapy [2,6]. Elevated liver enzymes occurred in 3%, which generally resolved or stabilized after re-testing. These results suggest that bempedoic acid may be a viable option for patients who cannot tolerate higher doses of statins.

In addition to efficacy and tolerability, once-daily oral administration and relatively lower cost (compared to PCSK9 inhibitors) make bempedoic acid an attractive option for more intensive LDL-C management [5]. Current guidelines increasingly emphasize strict LDL-C targets in high-risk groups, and many patients remain above these targets on statin therapy alone [1,7,15]. While vigilance regarding hepatic transaminases and glycemic control is essential, especially in high-risk patients, the overall risk–benefit profile appears favorable.

Limitations include single-centre design, a modest sample size of 200 patients that may limit generalizability of our findings. Also, the follow-up duration is 12 months; thus, to derive conclusions on long-term cardiovascular outcomes, longer follow-up is required. Randomized controlled trials with higher cohort size and longer observation periods are needed to more clearly establish a role for bempedoic acid in the setting of secondary prevention of CAD [9].

To these studies, there remains bempedoic acid: this added on to existing statin treatment further reduced levels of LDL cholesterol. On its own it raised few safety signals but promising to be added into patients being treated for primary or secondary lipid reduction as who is unable or is intolerance on existing statins.

CONCLUSION

In conclusion, Bempedoic acid as an adjunct to statin therapy offers a clinically meaningful reduction in LDL-C levels and a reassuring safety profile in patients with established CAD. The magnitude of LDL-C lowering, combined with tolerability and convenience, positions Bempedoic acid as a promising option for high-risk populations who struggle to reach guideline-recommended lipid targets on statins alone. Our findings support the growing consensus that Bempedoic acid can fill a critical gap in comprehensive secondary prevention strategies, particularly for those with statin intolerance or insufficient LDL-C response. Further large-scale, long-term studies are warranted to confirm these benefits.

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