ORIGINAL ARTICLE

Elobixibat and Lipid Regulation: A Study of Novel Strategy for Lowering Low-Density Lipoprotein and Raising High-Density Lipoprotein Using Drug Elobixibat

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Abstract

Background: Chronic constipation and dyslipidemia are common health problems that often coexist because of overlapping pathophysiologic mechanisms. Elobixibat is an ileal bile acid transporter inhibitor with promising effects on gastrointestinal motility and lipid metabolism. **Objectives**: This study aimed to evaluate the efficacy of elobixibat in improving lipid profiles by increasing high-density lipoprotein (HDL) levels and reducing low-density lipoprotein (LDL) levels. In addition, to assess its potential as a treatment for those with both concomitant chronic constipation and dyslipidemia. **Methods**: A randomized controlled trial was performed in 50 adults aged 30–65 years with chronic constipation and dyslipidemia. Participants received elobixibat 10 mg once daily for 4 weeks. Lipid profiles and frequency of bowel movement were measured before and after treatment. Statistical analysis was done using paired t-tests, and significance was set at $P < 0.05$. **Results**: Analysis of pre- and post-treatment values showed a significant decrease in LDL levels (mean decrease 18.6 mg/dL, $P < 0.001$) and a significant increase in HDL levels (mean increase 5.2 mg/dL, $P = 0.003$). There were also improvements in bowel frequency. **Conclusion**: Elobixibat has the dual benefits of enhancing bowel motility and significantly improving lipid profiles. These findings suggest its potential as a novel therapeutic agent for metabolic and gastrointestinal comorbidities.

Key words: Bile acid, chronic constipation, dyslipidemia, elobixibat, high-density lipoprotein, low-density lipoprotein, lipid metabolism

INTRODUCTION

A considerable percentage of adults worldwide suffer from chronic constipation and dyslipidemia, two common public health issues. Characterized by increased triglycerides, reduced levels of high-density lipoprotein-cholesterol (HDL-C), and higher levels of low-density lipoprotein-cholesterol (LDL-C), dyslipidemia is a significant modifiable risk factor for cardiovascular illnesses. It has a role in the development of coronary artery disease, atherosclerosis, and cerebrovascular events – all of which continue to be major causes of death globally.[1,2] Conversely, up to 20% of people worldwide suffer from persistent

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constipation, a common gastrointestinal ailment that is particularly prevalent in women and the elderly.[3] Chronic constipation is not fatal, but it significantly lowers quality of life, increases healthcare use, and is linked to other metabolic diseases such as obesity and dyslipidemia.[4]

Constipation and dyslipidemia have historically been treated as distinct clinical disorders. Recent developments in the study of the gut–liver axis and molecular biology, however, indicate that the two may have similar pathways, especially in relation to the metabolism of bile acids.[5] The liver produces bile acids from cholesterol, which are essential for maintaining cholesterol homeostasis and absorbing fat. Bile acid availability in the gut is controlled by enterohepatic circulation, and its signaling pathways affect gastrointestinal motility as well as lipid metabolism.[6]

Elobixibat is a first-in-class inhibitor of the ileal bile acid transporter (IBAT) that blocks bile acid reabsorption in the terminal ileum. This results in an accumulation of bile acids in the colon, stimulating secretion of fluid and peristalsis, relieving constipation. At the same time, elobixibat reduces blood LDL-C levels by increasing the conversion of cholesterol to bile acids in the liver and inhibiting the absorption of bile acids. In addition, some studies show that it could positively change HDL-C levels.[7-9] Elobixibat has previously been shown in studies to be effective for improving bowel movements in people with chronic idiopathic constipation. However, little is known about its effects on lipid metabolism, especially in people with already existing dyslipidemia. Gaining insight into Elobixibat's twin advantages may pave the way for patients with both illnesses to get integrated care.

The aim of this randomized controlled experiment was to evaluate the extent to which elobixibat modifies the lipid profile, specifically lowering LDL-C and increasing HDL-C levels. The study also evaluates its therapeutic potential to improve bowel habits in patients with dyslipidemia and persistent constipation. The present study explores a novel treatment concept in internal medicine and preventive cardiology by the application of one pharmacologic substance against two common diseases.

MATERIALS AND METHODS

Source of data

The study was conducted using the primary data collected from the patients visiting the gastroenterology and internal medicine outpatient departments of Saveetha Medical College and Hospital.

Study design

This was a prospective, open-label, randomized controlled trial in a single center to investigate the effects of elobixibat on lipid metabolism and bowel function.

Study location

The study was conducted at Saveetha Medical College and Hospital, a tertiary care academic institution with dedicated clinics for gastroenterology and metabolic disorders.

Study duration

The study was carried out over a period of 6 months, from August 2024 to February 2025, including recruitment, follow-up, and analysis.

Sample size

A total of 50 patients were recruited based on sample size calculation derived from previous studies showing expected differences in lipid parameters with elobixibat therapy (alpha = 0.05, power = 80%).

Inclusion criteria

- Adults aged 30–65 years
- Diagnosed with chronic constipation (Rome IV criteria)
- Dyslipidemia (LDL-C >130 mg/dL and/or HDL-C <40 mg/dL in men, <50 mg/dL in women)
- Not on lipid-lowering agents in the last 3 months
- Provided informed consent.

Exclusion criteria

- Inflammatory bowel disease or bowel obstruction
- Severe hepatic or renal impairment
- History of gastrointestinal surgery
- Pregnancy or lactation
- Use of bile acid sequestrants or antibiotics affecting gut flora.

Procedure and methodology

Patients who met eligibility requirements were enrolled following the acquisition of signed informed consent. For 4 weeks, they were randomized to receive 10 mg of elobixibat orally once a day before breakfast. During the research, no additional drugs for dyslipidemia or constipation were allowed. A thorough history, physical examination, and blood samples for the fasting lipid profile (LDL-C, HDL-C, total cholesterol, and triglycerides) were all part of the baseline evaluations. The Bristol Stool Form Scale and a bowel diary were used to record the frequency of bowel movements and the consistency of the stool. All evaluations were conducted again following 4 weeks of treatment. Weekly follow-ups by phone or in person were used to monitor patients and evaluate compliance and side effects.

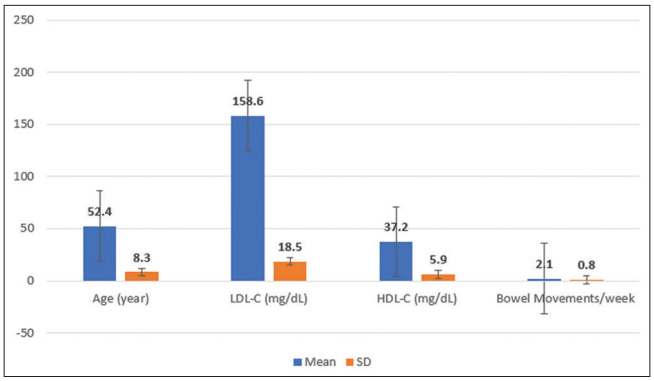

Figure 1: Baseline clinical parameters of the study participants (mean ± SD)

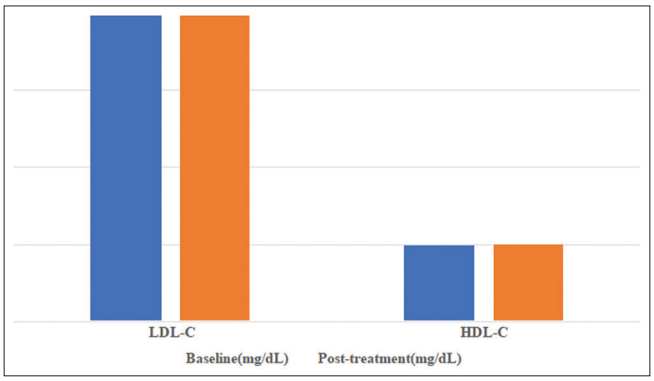

Figure 2: Comparison of baseline and post-treatment LDL-C and HDL-C levels

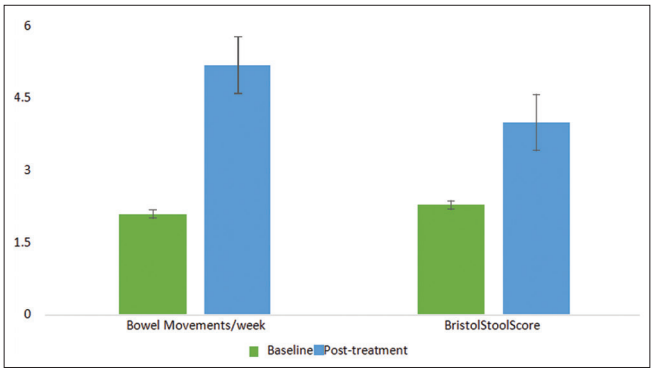

Figure 3: Comparison of bowel function parameters at baseline and post-treatment

Statistical methods

Statistical analysis was performed using the Statistical Package for the Social Sciences version 26.0. Descriptive statistics were used for baseline characteristics. Paired *t*-tests were used to compare pre- and post-treatment lipid values and bowel frequency. $P < 0.05$ was considered statistically significant.

Data collection

All clinical data, including demographic details, lipid profiles, bowel movement logs, and side effects, were recorded in a structured data collection form by trained research staff.

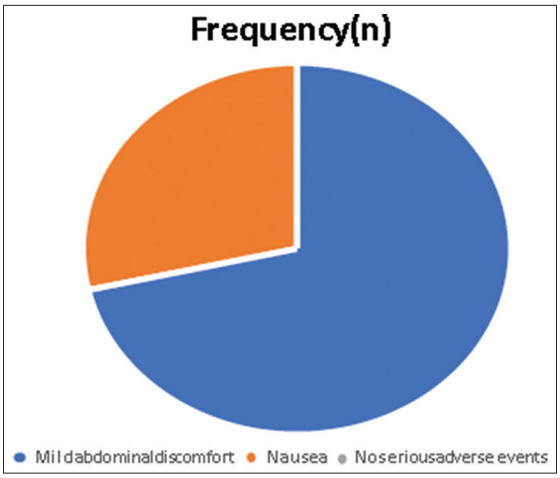

Figure 4: Frequency of adverse events reported during elobixibat treatment

Table 1: Baseline characteristics of study participants (*n*=50)

Variable	Mean±standard deviation/*n* (%)
Age (years)	52.4±8.3
Gender (Male/Female)	22 (44%)/28 (56%)
Low-density lipoprotein cholesterol (mg/dL)	158.6±18.5
High-density lipoprotein cholesterol (mg/dL)	37.2±5.9
Bowel movements/Week	2.1±0.8

RESULTS

The demographic and baseline clinical characteristics of the 50 patients who were enrolled in the randomized controlled experiment are shown in Table 1. The mean baseline values of age, LDL-C, HDL-C, and bowel movement frequency are illustrated in Figure 1. The participants were middle-aged, with an average age of 52.4 ± 8.3 years. With 56% of the population being female (n = 28) and 44% being male (n = 22), the gender distribution was rather skewed. The study population had dyslipidemia, as evidenced by the mean LDL-C of 158.6 ± 18.5 mg/dL and the mean HDL-C of 37.2 ± 5.9 mg/dL at baseline. According to the Rome IV criteria, chronic constipation was confirmed by the average frequency of bowel movements, which was 2.1 ± 0.8/week.

The Table 2 demonstrates the changes in lipid parameters before and after 4 weeks of treatment with 10 mg of elobixibat daily. The statistically substantial improvement in the atherogenic lipid load was reflected by the remarkable drop in LDL-C values from 158.6 ± 18.5 mg/dL to 140.0 ± 17.4 mg/dL (mean change −18.6 mg/dL, $P < 0.001$). At the same time, HDL-C levels increased from 37.2 ± 5.9 mg/dL to 42.4 ± 6.1 mg/dL, an average of +5.2 mg/dL, which was likewise statistically significant ($P = 0.003$). The changes in

Table 2: Changes in lipid profile post-treatment

Lipid parameter	Baseline (mg/dL)	Post-treatment (mg/dL)	Mean change	*P*-value
Low-density lipoprotein cholesterol	158.6±18.5	140.0±17.4	−18.6	<0.001
High-density lipoprotein cholesterol	37.2±5.9	42.4±6.1	+5.2	0.003

Table 3: Bowel function improvements

Parameter	Baseline	Post-treatment	*P*-value
Bowel movements/week	2.1±0.8	5.2±1.2	<0.001
Bristol stool score	2.3±0.7	4.0±0.6	<0.001

Table 4: Reported adverse events

Adverse event	Frequency (*n*)
Mild abdominal discomfort	5
Nausea	2
No serious adverse events	0

LDL-C and HDL-C levels from baseline to post-treatment are shown in Figure 2. These data demonstrate that elobixibat has two metabolic benefits on the lipid profile.

The effectiveness of elobixibat in enhancing bowel habits is shown in Table 3. The medication led to a significant increase in the number of bowel movements (2.1 ± 0.8–5.2 ± 1.2/week, $P < 0.001$) with satisfactory relief of constipation. Furthermore, stool consistency (Bristol stool score) changed from baseline 2.3 ± 0.7 to 4.0 ± 0.6 after therapy ($P < 0.001$), indicating a shift from lumpy, hard stools to more normal, soft, sausage-shaped stools. The changes in bowel movement frequency and Bristol Stool Score from baseline to post-treatment are shown in Figure 3. The results indicated that elobixibat was effective in improving gastrointestinal motility and stool quality.

The safety profile of elobixibat during the 4-week treatment period is summarized in Table 4 and Figure 4. Mild abdominal discomfort was reported by five participants, and nausea by two participants. Importantly, no serious adverse events were reported in the study, thus showing the tolerability and safety of the drug in the study population. In summary, these data indicate that elobixibat is a well-tolerated treatment with minor and self-limited adverse effects.

DISCUSSION

This randomized controlled experiment assessed the efficacy of elobixibat in relieving symptoms of chronic constipation and improving lipid profiles, particularly in reducing LDL-C and elevating HDL-C values. These findings highlight the dual potential of elobixibat to be an attractive therapeutic agent that could provide a novel and comprehensive approach to the management of patients with concomitant gastrointestinal and metabolic disorders.

Impact on lipid profile

The most prominent result of this study was the significant reduction in LDL cholesterol levels and increase in HDL cholesterol levels after 4 weeks of elobixibat treatment. The mean levels of LDL-C decreased from 158.6 mg/dL to 140.0 mg/dL ($P < 0.001$), and HDL-C increased from 37.2 mg/dL to 42.4 mg/dL ($P = 0.003$). These changes are of importance both statistically and clinically.

Elobixibat works by modulating lipids through inhibition of the IBAT. Elobixibat inhibits the reabsorption of bile acids and increases the amount of bile acids excreted in feces. This loss is counterbalanced by an increased hepatic conversion of cholesterol to bile acids with a subsequent reduction in blood LDL levels.[10,11] In addition, the decrease in the bile acid pool stimulates the signaling pathways of liver X receptor and farnesoid X receptor, which are known to have favorable effects on HDL metabolism.[12]

These results are consistent with previous pharmacodynamic investigations that showed that elobixibat decreased both total and LDL-C.[13] The evidence supporting its usefulness in patients with dual pathologies is strengthened by the fact that our study is one of the first to precisely evaluate these alterations in a population with concomitant dyslipidemia and persistent constipation.

Improvement in bowel function

The increase in weekly bowel movements and improvement in Bristol Stool Scale scores ($P < 0.001$ for both) indicate that elobixibat significantly improved stool consistency and frequency in addition to lipid management. This is in line with other studies that confirmed elobixibat's effectiveness in treating persistent idiopathic constipation. The mechanism here is the rise of bile acids in the colon, which stimulates water and chloride secretion and improves colonic motility, thereby acting as natural laxatives. The use of elobixibat in patients with metabolic syndrome and associated gastrointestinal motility issues is justified by this dual action, Silos-Santiago *et al*.[14]

Therapeutic implications

Elobixibat's dual action provides important therapeutic benefits. Elobixibat provides a single-agent treatment for

patients with chronic constipation and dyslipidemia, a frequent clinical overlap, especially in obese or older people. This might improve adherence and lessen the requirement for polypharmacy. Furthermore, as cardiovascular disease continues to be a major source of morbidity and death worldwide, any strategy that improves lipid profiles and provides extra systemic benefits deserves careful thought. Since there are not many pharmacologic treatments that dramatically raise HDL-C, the observed increase in HDL-C levels is quite noteworthy.[15]

Safety and tolerability

Only a few minor side effects, such as moderate stomach pain and temporary nausea, were recorded, and elobixibat was usually well tolerated. Every subject finished the 4-week course of therapy, and no significant side effects occurred. In line with earlier Phase II and III trials, this positive safety profile.

Comparison with existing therapies

Even while statins are still the mainstay of treating dyslipidemia, intolerance can occasionally restrict their usage, especially in older persons and people with other comorbidities. Due to its unique action, elobixibat may be used as a supplement or substitute for statins in patients who cannot take them or who need extra lipid-lowering effects without being exposed to systemic drugs.[16] In addition, it differs from other medications such as ezetimibe or PCSK9 inhibitors, which do not treat gastrointestinal symptoms, due to its distinct effect on both cholesterol and bowel function. Pharmacologically speaking, treating two illnesses with a single medication may save medical expenses and enhance patient outcomes.[17-19]

Limitations in the context of current literature

Although encouraging, the results of this study need to be viewed in light of its limitations, which are covered in more detail below. Furthermore, as is well-established for statins and other lipid-lowering drugs, larger, longer-term trials are needed to determine if the lipid-lowering effect of elobixibat is associated with a reduction in cardiovascular risk.

Future directions

Future research should emphasize on:

- Reproduce these findings in multicenter studies with larger and more heterogeneous populations
- Investigate the chronic cardiovascular consequences of elobixibat
- Study its role in combination therapy with statins or fibrates.
- Look at the effect on other metabolic measures such as insulin sensitivity and liver fat content.

Limitations of the study

1. Short duration: However, due to the duration of the study (4 weeks), we could not evaluate cardiovascular outcomes or long-term changes in lipid profile.
2. Small sample size: Although 50 patients were the trial's maximum size, this may have left out less frequent side events or subgroup differences, even though it was enough for initial effectiveness.
3. Open-label design: Subjective measurements such as bowel habits may be biasedly reported due to the absence of blinding.
4. Single center: The generalizability of the study findings to larger populations may be limited because the study was conducted at a single tertiary care center.
5. Lack of control group: To support causal inference, there should have been an active comparator arm or a placebo.
6. Lack of dietary intake assessment: Although diet has a major impact on cholesterol levels and intestinal function, it was not examined in this study.

CONCLUSION

Elobixibat, a new IBAT inhibitor, has been shown in this trial to effectively cure chronic constipation while also drastically altering lipid profiles. During a 4-week treatment period, elobixibat effectively decreased LDL-C levels and raised HDL-C levels in our randomized study of 50 persons with coexisting dyslipidemia and constipation. Significant improvements in bowel function coincided with these lipid changes, indicating a strong dual mechanism of action.

A promising tactic in modern clinical practice is elobixibat's capacity to utilize bile acid physiology for dual therapeutic results. Targeting such overlapping systems may not only be effective but also efficient, given the similar pathophysiology of gastrointestinal and metabolic illnesses, which are frequently supported by sedentary lifestyles and dietary habits. Patients who are over burdened by polypharmacy may find that elobixibat simplifies their therapy.

Regarding safety, there were no significant side effects and the medication was well taken. Additional benefits include its oral administration and low systemic absorption, especially in sick or elderly individuals. These features make elobixibat a strong contender for long-term treatment, but further study is warranted to demonstrate long-term efficacy and cardiovascular benefit.

The results of this study are encouraging; however, the results also suggest the need for further studies with multicenter trials and larger cohorts, longer follow-up, and comparator arms. The effect of elobixibat on a more comprehensive metabolic profile, such as insulin resistance and hepatic steatosis, can be potentially evaluated in future studies. In summary, elobixibat offers a novel and potentially transformative approach to the management of

chronic constipation and dyslipidemia, two common conditions that are often treated individually. Its inclusion in clinical recommendations may herald a shift to more comprehensive, mechanism-based therapies that take the complexities of caring for chronic illnesses in today's world into consideration.

AUTHOR'S CONTRIBUTIONS

Vimal S, Ethihas Reddy M, and Kedari G.S.R: conception and design of the review, literature search, analysis; Kaloni K. Subramani, Mathesh Athinarayanan, and Parthiban P: interpretation, manuscript writing, revision, formal analysis, validation, and writing.

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