Exploring the Treatment Outcomes and Safety of Elobixibat for Chronic Constipation: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Maggie Liberty[1], Taufik Sungkar[2], Peggy Liberty[1]

[1]Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia.
[2]Division of Gastroenterology-Hepatology, Department of Internal Medicine, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia.

Corresponding Author:
Taufik Sungkar, MD., PhD. Division of Gastroenterology-Hepatology, Department of Internal Medicine, Faculty of Medicine, Universitas Sumatera Utara. Jl. Dr. Mansyur No.5, Padang Bulan, Medan 20155, Indonesia. Email: taufik.sungkar@usu.ac.id.

ABSTRACT

Background: *Currently available laxatives usage in chronic constipation (CC) has been reported to cause various adverse events, notably melanosis coli and colonic neuromuscular disorder. Elobixibat, an ileal bile acid transporter inhibitor, appears to be a promising option for chronic constipation to counteract this challenge. This study aims to evaluate the treatment outcome and safety of elobixibat for chronic constipation.* ***Methods:*** *This systematic review and meta-analysis were performed on 3 search engines: PubMed/MEDLINE, ScienceDirect, and Cochrane Database of Systematic Reviews. Randomized controlled trials (RCTs) comparing elobixibat 10 mg with placebo in patients with functional chronic constipation were included. The quality of studies was assessed using the Cochrane risk of bias 2.0 tool. Statistical analyses were conducted using RevMan 5.4.1 software.* ***Results:*** *A total of six RCTs that met the inclusion criteria were included in this study. Results demonstrated that elobixibat markedly improved bowel movement with a significant change in spontaneous bowel movement (SBM) (MD 2.91, 95% CI 2.81 to 3.01, p<0.00001) and complete spontaneous bowel movement (MD 0.61, 95% CI 0.38 to 0.83, p<0.00001). The percentage of patients experiencing first SBM in 24 hours was significantly higher in the elobixibat group compared to the placebo group (RR 1.49, 95% CI 1.21 to 1.84, p=0.0002). Stool consistency was improved significantly in the elobixibat group (MD 1.40, 95% CI 1.09 to 1.71, p<0.00001). Moreover, the elobixibat group reported a favourable safety with no serious adverse events.* ***Conclusion:*** *Elobixibat shows promising therapeutic efficacy in the treatment of functional chronic constipation. Elobixibat is safe and well-tolerated with minimal adverse events.*

Keywords: *chronic constipation, laxatives, elobixibat.*

INTRODUCTION

Chronic constipation (CC) is among the most prevalent gastrointestinal disorders, affecting 10−15% of the population worldwide.[1] Chronic constipation is more frequent in female and Asian populations, increases with age, and correlates with a sedentary lifestyle and low-fiber diets.[2] According to the Rome criteria, CC is a condition characterized by infrequent bowel movement, difficult stool passage, hard lumpy stool, sensation of incomplete bowel evacuation, and straining during defecation over a period of at least 3 months.[3] It is often associated with other symptoms, including urinary and sexual dysfunction. Hence, the condition may impact the quality of life of patients and limit work productivity, adding to the social burden.[4]

Standard management strategies for CC rely on lifestyle and dietary modification combined with laxative use. Currently available laxatives include bulk-forming agents and osmotic, stimulant, and lubricant laxatives.[5] Regarding laxatives, the first treatment option is generally osmotic or stimulant laxatives. However, chronic laxative use is reported to cause various adverse events. Long-term use of stimulant laxatives, particularly the widely used anthraquinone-containing laxatives, is often associated with melanosis coli, a condition characterized by colonic mucosal hyperpigmentation.[6] Additionally, precautions must be taken when using some laxatives, particularly osmotic laxatives, for patients with kidney and liver comorbidities. Moreover, adverse events such as metabolic disturbance, headache, nausea, diarrhea, cardiovascular disorders, and colonic neuromuscular disorder leading to the loss of haustral folds in the colon, have been reported following chronic usage of common laxatives.[7] Therefore, there is a need for novel alternatives with distinct mechanisms of action.

Elobixibat, a novel selective inhibitor of ileal bile acid transporter (IBAT), inhibits IBAT expression in epithelial cells in the terminal ileum, disrupting bile acid (BA) enterohepatic circulation and upregulating hepatic bile acid production.[8] It increases BA concentrations in the colon, resulting in accelerated colonic transit and secretion and improved bowel movements.[9] Through this mechanism of action, elobixibat offers a novel therapy for chronic constipation. Recently, the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) approved elobixibat 10 mg once daily as a treatment option for chronic constipation.[10] However, the evidence regarding its clinical efficacy and safety remains insufficient.

The objective of our study was to evaluate the treatment outcomes and safety of elobixibat at the dose of 10 mg once daily as a treatment for chronic constipation, focusing on improvements in bowel movement and stool consistency.

METHODS

Search Strategy

A literature search was carried out using the keywords “chronic constipation”, “laxative”, and “elobixibat” in the three databases ScienceDirect, PubMed/MEDLINE, and Cochrane Library to identify studies up to the year 2025. The keywords were submitted to the advanced search option of the databases, incorporating the Boolean operators OR and AND to obtain synonym results in accordance with the Medical Subject Headings (MeSH) terms and the results of the specified keywords. Therefore, the applied search terms became: (“constipation” OR “chronic constipation”) AND (“laxative” OR “elobixibat” OR “ileal bile acid inhibitor” OR “IBAT”). The protocol for this review was registered on 4th August 2025 in the International Prospective Register of Systematic Reviews (PROSPERO) with identification number CRD420251118926.

Eligibility Criteria

The eligibility criteria for this systematic review were randomized controlled trials (RCTs) with patients diagnosed with chronic constipation based on the Rome II, III, or IV criteria. Included studies evaluated the efficacy and safety of elobixibat using the recommended 10 mg dosage and a control group receiving a placebo as a comparison. The studies were required to report outcomes including stool frequency, assessed using spontaneous bowel movement (SBM) and/or complete spontaneous bowel movement (CSBM) numbers, stool consistency, assessed using the Bristol Stool Form Scale (BSFS), and adverse events to assess the safety profile. Eligible studies were in English, and the full text had to be accessible.

Excluded studies were those that included participants younger than 18 years old, patients with organic constipation or with a history of intestinal surgery, or pregnant and/or lactating women. Animal studies, reviews, case reports, editorials, duplicates, and studies with insufficient data, such as missing baseline or follow-up data, were excluded.

Study Selection

This systematic review and meta-analysis were performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[11] All the authors conducted the comprehensive searches and removed detected duplicates. The identified studies were manually screened based on title and abstract. Each article deemed relevant and within the scope of this systematic review was selected for further evaluation. Each author conducted a full-text review of the selected studies that passed the initial screening to confirm their eligibility.

Quality Assessment

The Cochrane Risk of Bias 2.0 tool (RoB 2) was utilized to assess the quality of the RCTs included in this study. The tool has five domains through which the risk of bias can be categorized as 'low', 'high', or 'some concerns'.[12] Two authors independently rated each eligible full-text article. Disagreement between the authors' assessments was discussed and resolved by a third author.

Data Collection Process and Outcome Measures

The studies that fulfilled the inclusion criteria were analyzed, and data were synthesized narratively. Data extracted from the studies were the following: the name of the main author, the year and site of publication, sample sizes, inclusion and exclusion criteria of the samples, number of patients treated with elobixibat or in the control group, outcomes of the patients treated with elobixibat or control, and baseline characteristics of the samples. The main outcomes for this study were the improvement of symptoms evaluated through the mean change in bowel movement, assessed using spontaneous bowel movement (SBM) and complete spontaneous bowel movement (CSBM) numbers, and the proportion of patients having their first SBM within 24 hours. SBM was defined as the number of spontaneous bowel movements per week without laxative use within the last 48 hours, whereas CSBM was the number of SBM with the feeling of complete evacuation.[13] The secondary outcomes were stool consistency, assessed using the Bristol Stool Form Scale (BSFS), and adverse events. The BSFS is a diagnostic tool that classifies stool consistency into 7 types, from hard lumpy stool (type 1) to watery stool (type 7).[14]

Statistical analyses were conducted using RevMan 5.4.1 software. Outcomes of the studies were pooled as mean deviation (MD) or prevalence with 95% confidence intervals (CI). The outcomes were defined as statistically significant if the p-value was < 0.05.

RESULTS

Study Selection

The study selection process of this review is outlined in the PRISMA flowchart shown in **Figure 1**. A total of 452 studies were identified following comprehensive searches in the three databases. Thirty-eight studies identified as duplicates were removed. Initial screening was conducted of 414 studies, excluding 386 studies that had irrelevant titles and abstracts, did not meet the inclusion criteria, and were in languages other than English. The remaining 32 studies were sought for retrieval, 7 of which could not be retrieved. The final 25 studies were appraised for eligibility. Consequently, a further 19 studies were eliminated, 9 of which presented different study models, 5 were meeting abstracts, 3 were editorial comments, and 2 were review articles. As a result, a total of 6 studies that met the eligibility criteria were included in this systematic review and meta-analysis.

Quality of the RCTs

The quality assessment for the studies included was carried out using the RoB 2 tool. Among the 6 RCTs included, 1 study was considered to be of 'some concern' due to missing outcome data. The others were indicated to have a low risk of bias. Results of the quality assessment of the included studies are summarized in **Figure 2.**

Baseline Characteristics of the RCTs

The baseline clinical and demographic characteristics of the studies are summarized in **Table 1**. This review comprised 6 RCTs, with a total of 526 patients diagnosed with chronic constipation. Among all the study populations, 271 patients were treated with elobixibat, while 255 patients received a placebo as a control

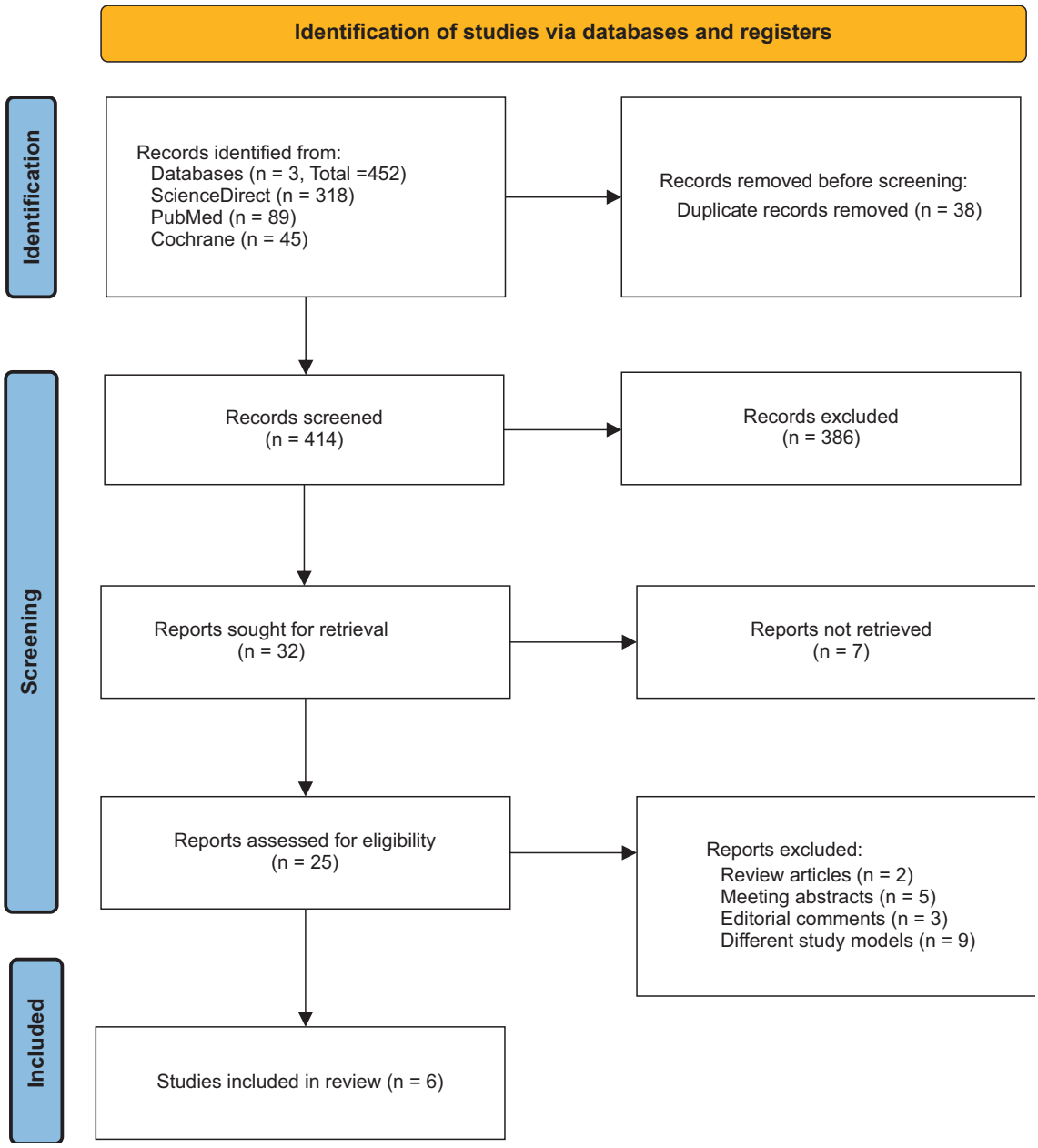

Figure 1. PRISMA flowchart.

group. The average age of the patients was 45 years, ranging from 30 to 60 years. The majority of the patients were female, accounting for approximately 66% of the total participants, indicating a higher prevalence of chronic constipation in females than in males. The baseline mean number of SBM per week was 1.75, ranging from 0.6 to 2.9. Most participants had a normal body mass index (BMI), but the population presented a tendency toward excess weight, with an approximate BMI range of 20–24 kg/m^2.

The participants were diagnosed with chronic constipation based on the Rome III or IV criteria. Patients with organic constipation, a history of intestinal obstruction, previous intestinal surgery, or other systemic comorbidities were deemed ineligible as study participants. The inclusion and exclusion criteria for participants were similar across all the studies, requiring adults with functional chronic constipation and no comorbidities. In the intervention group, patients were administered 10 mg elobixibat, with dosages ranging from 5 to 15 mg based

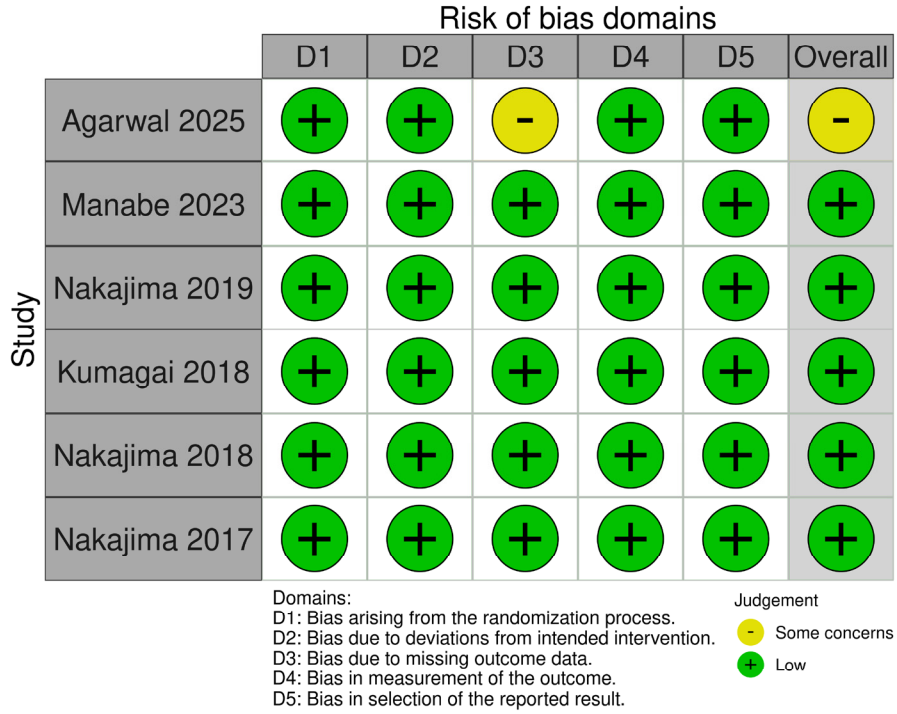

Figure 2. RoB-2 for RCT quality assessment.

on patient tolerance, for 2 weeks. In the control group, patients received a placebo. Outcomes extracted were the improvements in bowel movement parameters, stool consistency, and adverse events.

Bowel Movements

Bowel movements were assessed using SBM, CSBM, and the first SBM within 24 hours, as shown in **Figure 3**.

Spontaneous Bowel Movement (SBM)

Figure 3A illustrates the pooled results of mean changes in weekly SBM. Patients treated with elobixibat presented a significant increase in mean SBM number per week (MD 2.91, 95% CI 2.81 to 3.01, $p < 0.00001$) compared to patients treated with placebo.

Complete Spontaneous Bowel Movement (CSBM)

Figure 3B shows the mean changes in weekly CSBM. Patients treated with elobixibat presented a significant increase in mean CSBM number per week (MD 0.61, 95% CI 0.38 to 0.83, $p < 0.00001$) compared to patients treated with placebo.

First SBM within 24 hours

The pooled proportion of patients with the first SBM within 24 hours is depicted in Figure 3C. In the elobixibat group, the proportion of patients whose first SBM was within 24 hours was significantly greater (RR 1.49, 95% CI 1.21 to 1.84, $p = 0.0002$) than that in the placebo group.

Stool Consistency

The mean changes in BSFS values are presented in **Figure 4**. The stool consistency was remarkably improved in the elobixibat group, with a significant change in the mean BSFS (MD 1.40, 95% CI 1.09 to 1.71, $p < 0.00001$) compared to the placebo group.

Adverse Events

The analysis of the adverse events is shown in **Figure 5**. The incidence of adverse events was significantly higher in the elobixibat group (RR 1.56, 95% CI 1.02 to 2.38, $p = 0.04$) compared to the placebo group.

Table 1. Clinical characteristics and baseline demographics of the included studies

Study authors, year, design, location	Sample size (n)	Participants						Intervention				
		Age, year (mean, SD)	Gender (n)	BMI, kg/m2 (mean, SD)	Number of SBM /week (mean, SD)	Diagnosis of CC	Exclusion criteria	Dose of Elobixibat	Treatment duration	Control	Outcomes	Follow up
Agarwal et al., 2025.[15] RCT, India.	146 E: 75 C: 71	E: 42.1 ± 12.80 C: 38.2 ± 12.92	F: 48 M: 98	E: 24.5 ± 4.64 C: 24.0 ± 4.40	N/I	Rome IV criteria	CVD, liver, renal, or psychiatric disorders, ADR, pregnant and breastfeeding, or organic disorder	10 mg oral, once daily, before a meal	2 weeks	Placebo	First 24 hours SBM, AEs	2 weeks
Manabe et al., 2023.[16] RCT, Japan	17 E: 9 C: 8	E: 69 ± 5.2 C: 67 ± 3.7	F: 8 M: 9	E: 65.1 ± 9.6 C: 49.9 ± 14.6	N/I	Rome IV criteria	Organic disorder, biliary obstruction, severe renal or hepatic disorder, CVD, allergy, malignancy	10 mg oral, once daily, before a meal	2 weeks	Placebo	SBM, CSBM	2 weeks
Nakajima et al., 2019.[17] RCT, Japan	132 E: 69 C: 63	E: 43.0 ± 13.7 C: 43.8 ± 13.0	F: 109 M: 23	E: 21.4 ± 2.6 C: 21.8 ± 2.7	E: 1.8 ± 0.9 C: 1.7 ± 1.0	Rome III criteria	Organic constipation, history of intestinal surgery	10 mg oral, once daily, before a meal	2 weeks	Placebo	SBM, CSBM	2 weeks
Kumagai et al., 2018.[18] RCT, Japan	20 E: 10 C: 10	35.4 ± 10.8	N/I	22.2 ± 2.5	1.7 ± 0.7	Rome III criteria	Organic, neurologic, medication, hormonal constipation, intestinal obstruction, intestinal surgery	10 mg oral, once daily, before a meal	2 weeks	Placebo	First 24 hours SBM, AEs	2 weeks
Nakajima et al., 2018.[10]	132 E: 69 C: 63	E: 43.0 ± 13.7 C: 43.8 ± 13.0	F: 109 M: 23	E: 21.4 ± 2.6 C: 21.8 ± 2.7	E: 1.8 ± 0.9 C: 1.7 ± 1.0	Rome III criteria	Organic, neurological, or endocrine disorders, or intestinal surgery	10 mg oral, once daily, before a meal	2 weeks	Placebo	SBM, first 24 hours, SBM, stool consistency, AEs	2 weeks
Nakajima et al., 2017.[19]	79 E: 39 C: 40	E: 43.4 ± 13.4 C: 44.9 ± 12.2	F: 73 M: 6	E: 21.93 ± 4.01 C: 21.40 ± 2.42	E: 1.6 ± 1.0 C: 1.8 ± 1.1	Rome III criteria	Organic constipation, or constipation due to an underlying disease	10 mg oral, once daily, before a meal	2 weeks	Placebo	SBM, CSBM, first 24 hours SBM, stool consistency, AEs	2 weeks

Abbreviations: BMI, body mass index; CC, chronic constipation; RCT, randomized controlled trial; E, elobixibat group; C, control group; F, female; M, male; CVD, cardiovascular disease; SBM, spontaneous bowel movement; CSBM, complete spontaneous bowel movement; AEs, adverse events

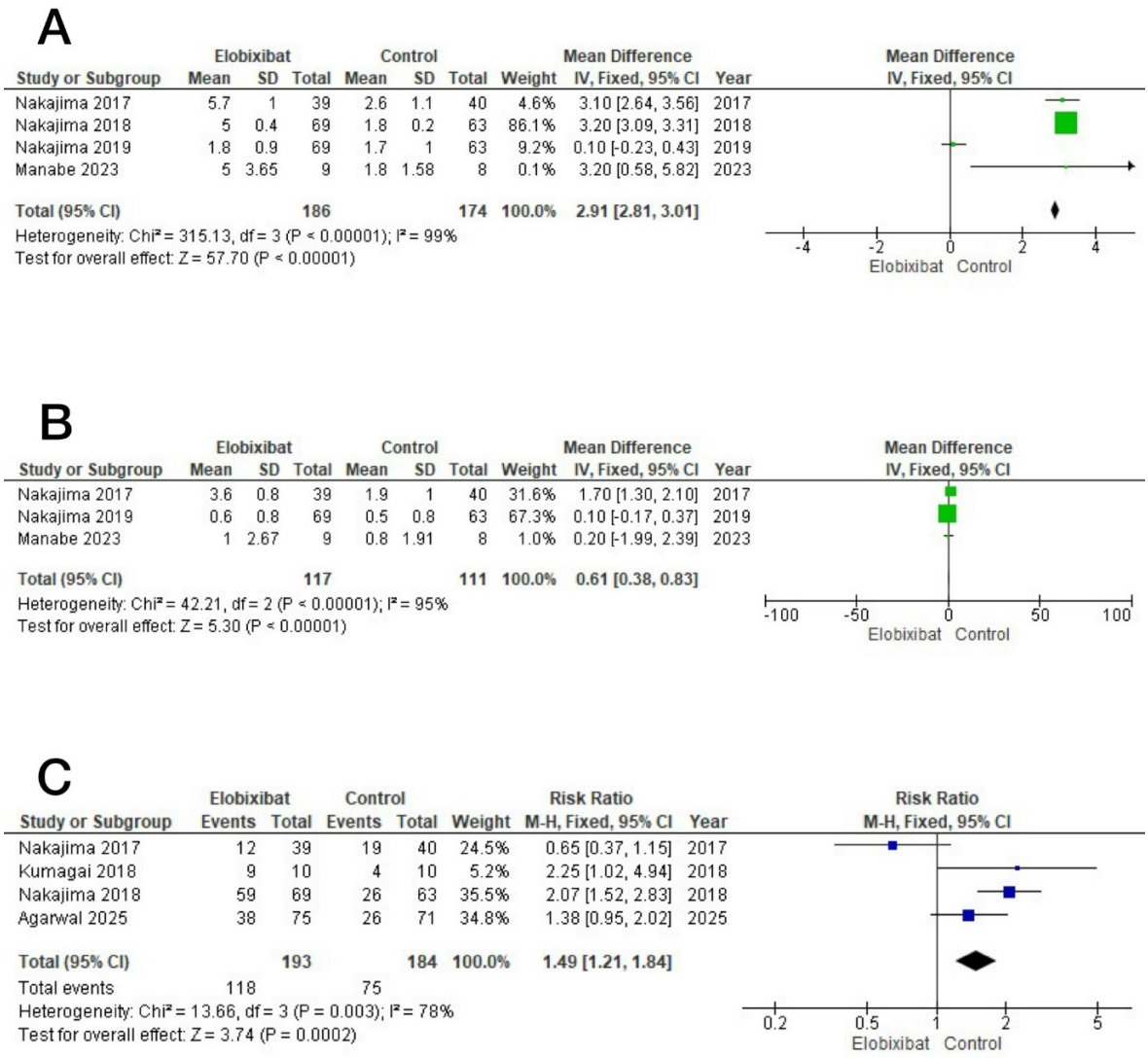

Figure 3. (A) Forest plot of mean changes in weekly SBM number; (B) Forest plot of mean changes in weekly CSBM number; (C) Forest plot of proportion of patients with first SBM within 24 hours.

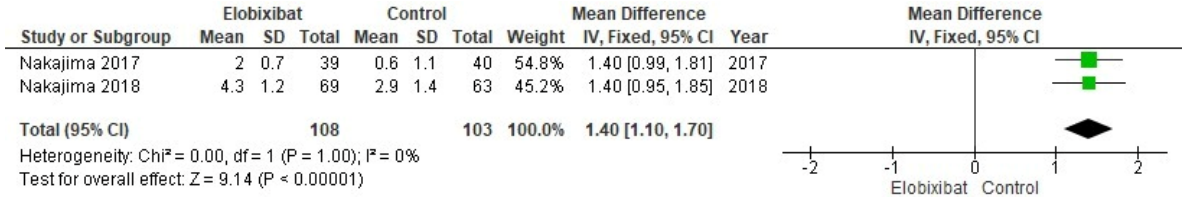

Figure 4. Forest plot of mean changes in Bristol Stool Form Scale.

Figure 5. Forest plot of the incidence of adverse events.

DISCUSSION

This systematic review and meta-analysis assessed improvements in chronic constipation symptoms based on changes in bowel movement and stool consistency in 526 patients receiving once daily elobixibat 10 mg compared to a placebo control group. Bowel movements and stool consistency were evaluated weekly, starting from 2 weeks after the first administration of elobixibat or placebo. Spontaneous bowel movement was significantly improved in patients receiving elobixibat. Agarwal et al. reported that patients receiving elobixibat experienced a markedly greater frequency of SBM, with a 1.15 difference compared to placebo.[15] The studies by Manabe et al. and Nakajima et al. also reported that elobixibat notably improved weekly SBM numbers compared to placebo, regardless of gender and age. [16,17]

Patients treated with elobixibat reported a higher frequency of complete spontaneous bowel movement than the placebo group. Agarwal et al. and Manabe et al. also reported that the number of weekly CSBM in the elobixibat group was notably greater than in the placebo group.[15,16] Manabe et al. also found that elobixibat significantly lowered the rectal sensory threshold, enabling patients to perceive a sensation of complete evacuation.[16] The proportion of patients experiencing the first SBM within 24 hours was greater in the elobixibat group than in the control group (61% and 40%, respectively). This aligns with the study by Kumagai et al. in which all patients treated with elobixibat had their first SBM within 24 hours, whereas only 40% of the placebo group experienced the same.[18]

The mechanism of elobixibat involves inhibition of the ileal bile acid transporter, reducing bile acid (BA) enterohepatic reabsorption in the colon. Elobixibat increases bile acid concentration in the colon, hence augmenting the total fecal bile acid concentration.[20] Manabe et al. observed a substantial increase in the total fecal BA concentration among patients receiving elobixibat.[16] Elevated BA concentrations enhance colonic transit by inducing colonic contractions.[21] Unabsorbed bile acids in the colon activate transmembrane G protein-coupled receptor 5 (TGR5) on epithelial cells. This activation leads to stimulation of the cystic fibrosis transmembrane conductance regulator (CFTR), promoting chloride secretion and triggering the release of 5-hydroxytryptamine (5-HT). The released 5-HT then stimulates submucosal sensory nerves, initiating peristalsis.[22]

Elobixibat displays high efficacy in improving bowel movement, both SBM and CSBM. A recent Bayesian network meta-analysis comparing novel treatments for chronic constipation suggested an indirect comparison of elobixibat, lubiprostone, linaclotide, and lactulose. The analysis reported that elobixibat outperformed other agents in enhancing bowel evacuation, with a mean increase in SBM of 5.69 over placebo, compared to 1.95 for linaclotide, 2.41 for lubiprostone, and no change for lactulose.[23] Another meta-analysis assessing the efficacy of elobixibat, prucalopride, linaclotide, and tegaserod reported that elobixibat presented significant efficacy compared to placebo and was comparable with other therapies. [24]

Regarding the secondary endpoint, elobixibat effected a substantial improvement in stool consistency, as evaluated using the BSFS. Nakajima et al. indicated a significant enhancement in BSFS scores in the elobixibat group, reporting averages of 4.3 for elobixibat and 2.9 for placebo.[10] An observational study by Sakai et al. also reported a notable enhancement in stool consistency upon treatment with elobixibat. The results showed that the mean BSFS increased from 2.286 to 3.995 in patients aged below 65, and from 2.217 to 3.800 in those older than 65, indicating improvement across all ages.[25] Odaka et al. also indicated that elobixibat significantly improved BSFS scores, with the mean scores increasing from 1.8 at baseline to approximately 4 after one week of treatment, sustained over an 8-week treatment duration.[26] Elobixibat was found to stimulate fluid and electrolyte secretion by elevating intraluminal BA concentration in the colon. Unabsorbed BA activates the chloride channel that triggers fluid secretion in the intestinal lumen, resulting in stool softening. [27]

Patients administered with elobixibat exhibited some adverse events related to the

intervention. Across all the studies, the reported adverse events were mild abdominal distension, abdominal pain, diarrhea, and dyspepsia. No serious adverse events were reported after the administration of elobixibat.[10,15,18,19] In a post-marketing safety analysis, adverse events were observed in 5.24% patients taking elobixibat. Most cases were mild, but one death was reported in an elderly patient with severe cardiovascular comorbidities, though no direct causal relationship with elobixibat could be established.[28] Several studies suggest elobixibat to be safe, even in patients with comorbidities. For example, for patients with chronic kidney disease undergoing hemodialysis, elobixibat did not affect serum albumin levels or electrolytes, unlike other laxatives reported to cause hypokalemia.[29] Elobixibat was determined to be safe for patients with heart failure and was found to reduce blood pressure, an increase in which can be linked to straining during constipation.[30]

This systematic review and meta-analysis had several limitations. First, the limited number of studies and participants constrained the generalizability of the findings. Eligible studies were limited to those that focused on RCTs and patients without any severe comorbidities. Second, high heterogeneity was observed among the studies. However, we were unable to identify any clinical factors from the studies that could have contributed to this significant heterogeneity. Future research, conducting larger and multicenter RCTs, is anticipated to further validate these findings. Additionally, future research should aim to establish standardized elobixibat administration, including optimal timing of administration and comparison with other alternatives. By addressing these limitations, we hope that future studies will provide further evidence for the use of elobixibat in the treatment of chronic constipation.

CONCLUSION

In summary, elobixibat, a novel ileal bile acid transporter (IBAT) inhibitor, proved beneficial for the treatment of chronic constipation. Elobixibat effectively relieved the symptoms of chronic constipation by enhancing bowel movement and improving stool consistency. Furthermore, elobixibat was well tolerated and exhibited a favorable safety profile with minimal adverse events.

ACKNOWLEDGMENTS

None.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

FUNDING

None to declare.

REFERENCES

1. Aziz I, Whitehead WE, Palsson OS, Törnblom H, Simrén M. An approach to the diagnosis and management of Rome IV functional disorders of chronic constipation. Expert Rev Gastroenterol Hepatol. 2020 Jan;14(1):39-46. doi: 10.1080/17474124.2020.1708718.
2. Daniali M, Nikfar S, Abdollahi M. An overview of interventions for constipation in adults. Expert Rev Gastroenterol Hepatol. 2020 Aug;14(8):721-732. doi: 10.1080/17474124.2020.1781617.
3. Włodarczyk J, Waśniewska A, Fichna J, Dziki A, Dziki Ł, Włodarczyk M. Current overview on clinical management of chronic constipation. *Journal of Clinical Medicine*. 2021; 10(8):1738. doi: 10.3390/jcm10081738
4. Barbara G, Barbaro MR, Marasco G, Cremon C. Chronic constipation: from pathophysiology to management. Minerva Gastroenterol (Torino). 2023 Jun;69(2):277-290. doi: 10.23736/S2724-5985.22.03335-6.
5. Ihara E, Manabe N, Ohkubo H, et al. Evidence-based clinical guidelines for chronic constipation 2023. Digestion. 2025;106(1):62-89. doi: 10.1159/000540912.
6. Tian C, Nasser YA. Melanosis coli. StatPearls - NCBI Bookshelf. 2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK493146/
7. Bashir A, Sizar O. Laxatives. StatPearls - NCBI Bookshelf. 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537246/
8. Hojo M, Shibuya T, Nagahara A. Management of chronic constipation: A comprehensive review. Intern Med. 2025 Jan 1;64(1):7-15. doi: 10.2169/internalmedicine.2867-23.
9. Ramakrishna BS. Inhibition of bile acid reabsorption as a treatment for constipation. Indian Journal of Gastroenterology. 2025 Feb 26. doi: 10.1007/s12664-025-01736-0.
10. Nakajima A, Seki M, Taniguchi S, et al. Safety and

efficacy of elobixibat for chronic constipation: results from a randomised, double-blind, placebo-controlled, phase 3 trial and an open-label, single-arm, phase 3 trial. Lancet Gastroenterol Hepatol. 2018;3:537–47. doi: 10.1016/S2468-1253(18)30123-7.

11. Page MJ, McKenzie JE, Bossuyt PM, et al. The 17 PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 18 2021 Mar 29; 372:n71. doi:10.1136/bmj.n71
12. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019; 366: l4898. doi: 21 10.1136/bmj.l4898
13. Haghbin H, Zakirkhodjaev N, Gangwani MK, Beran A, Lee-Smith W, Piper MH, Aziz M. Efficacy and safety of vibrating capsule in treatment of chronic idiopathic constipation: a systematic review and meta-analysis of randomized controlled trials. Transl Gastroenterol Hepatol. 2024 Jan 16;9:8. doi: 10.21037/tgh-23-64.
14. Shokouhi N, Mohammadi S, Ghanbari Z, Montazeri A. Development of a new version of the Bristol Stool Form Scale: translation, content validity, face validity, and reliability of the Persian version. BMJ Open Gastroenterol. 2022 Dec;9(1):e001017. doi: 10.1136/bmjgast-2022-001017.
15. Agarwal P, Jha BK, Somagoni J, et al. Efficacy and safety of elobixibat in patients with chronic constipation—A randomized, multicenter, double-blind, placebo-controlled, parallel-group study from India. Indian Journal of Gastroenterology. 2025 Feb 22. doi: 10.1007/s12664-024-01719-7
16. Manabe N, Umeyama M, Ishizaki S, et al. Elobixibat improves rectal sensation in patients with chronic constipation aged ≥60 years: a randomised placebo-controlled study. BMJ Open Gastroenterology. 2023 Nov 1;10(1):e001257. doi: 10.1136/bmjgast-2023-001257
17. Nakajima A, Taniguchi S, Kurosu S, Gillberg P, Mattsson JP, Camilleri M. Efficacy, long-term safety, and impact on quality of life of elobixibat in more severe constipation: Post hoc analyses of two phase 3 trials in Japan. Neurogastroenterology & Motility. 2019 Feb 21;31(5). doi: 10.1111/nmo.13571
18. Kumagai Y, Amano H, Sasaki Y, et al. Effect of single and multiple doses of elobixibat, an ileal bile acid transporter inhibitor, on chronic constipation: A randomized controlled trial. British Journal of Clinical Pharmacology. 2018 Jun 30;84(10):2393–404. doi: 10.1111/bcp.13698
19. Nakajima A, Seki M, Taniguchi S. Determining an optimal clinical dose of elobixibat, a novel inhibitor of the ileal bile acid transporter, in Japanese patients with chronic constipation: a phase II, multicenter, double-blind, placebo-controlled randomized clinical trial. Journal of Gastroenterology. 2017 Aug 24;53(4):525–34. doi: 10.1007/s00535-017-1383-5
20. Nakajima A, Ishizaki S, Matsuda K, Kurosu S, Taniguchi S, Gillberg PG, Mattsson JP, Hasunuma T, Camilleri M. Impact of elobixibat on serum and fecal bile acid levels and constipation symptoms in patients with chronic constipation. J Gastroenterol Hepatol. 2022 May;37(5):883-890. doi: 10.1111/jgh. 15800.
21. Ticho AL, Malhotra P, Dudeja PK, Gill RK, Alrefai WA. Bile acid receptors and gastrointestinal functions. Liver Res. 2019 Mar;3(1):31-39. doi: 10.1016/j.livres.2019.01.001.
22. Wald A. Bile acids and bowel function: Do they play a role in constipation-associated irritable bowel syndrome? Clin Gastroenterol Hepatol. 2018 Apr;16(4):486-487. doi: 10.1016/j.cgh.2017.11.021.
23. Nakajima A, Shoji A, Kokubo K, Igarashi A. A Systematic review and network meta-analysis on the efficacy of medications in the treatment of chronic idiopathic constipation in Japan. Gastroenterol Res Pract. 2021 Nov 30;2021:5534687. doi: 10.1155/2021/5534687.
24. Luthra P, Camilleri M, Burr NE, Quigley EMM, Black CJ, Ford AC. Efficacy of drugs in chronic idiopathic constipation: a systematic review and network meta-analysis. Lancet Gastroenterol Hepatol. 2019 Nov;4(11):831-844. doi: 10.1016/S2468-1253(19)30246-8.
25. Sakai Y, Tsuyuguchi T, Kumagai J, Ohyama H, Kaiho T, Ohtsuka M, Kato N. Efficacy of elobixibat for elderly patients with chronic constipation in a clinic. World J Gastrointest Pharmacol Ther. 2025 Jun 5;16(2):105801. doi: 10.4292/wjgpt.v16.i2.105801.
26. Odaka T, Tominaga K. Uncontrolled, Open-Label Pre-dinner administration of Elobixibat in Japanese adults with chronic constipation: A retrospective chart review. Curr Ther Res Clin Exp. 2020 Nov 16;93:100616. doi: 10.1016/j.curtheres.2020.100616.
27. Ikeda N, Taniguchi S, Seki M. Pharmacological characteristics and clinical study results of ileal bile acid transporter inhibitor elobixibat (GOOFICE®tablet 5 mg). *Folia Pharmacologica Japonica*. 2019;153:129–138 .
28. Nakajima A, Fujimaki M, Arai Y, Emori K. Safety and efficacy of Elobixibat, an ileal bile acid transporter inhibitor, in elderly patients with chronic idiopathic constipation according to administration time: Interim analysis of post-marketing surveillance. J Neurogastroenterol Motil. 2022 Jul 30;28(3):431-441. doi: 10.5056/jnm20263.
29. Shono T, Hyakutake H. Efficacy and safety of elobixibat in hemodialysis patients with chronic constipation: a retrospective study. Renal Replacement Therapy. 2020 Apr 21;6(1). doi: 10.1186/s41100-020-00267-y
30. Fujisue K, Ito M, Matsuzawa Y, et al. Open-label, single-center, single-arm study evaluating the efficacy and safety of elobixibat for chronic constipation in patients with heart failure. Circ Rep. 2024 Feb 17;6(3):55-63. doi: 10.1253/circrep.CR-23-0099.