PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

Title (Provisional)

The effects of the combined use of linaclotide and oral sulfate solution in bowel preparation for chronic constipation patients undergoing colonoscopy: protocol of a prospective, randomized, controlled, single-blind clinical trial from a single center in China

Authors

Guo, Chunmei; Wang, Jing; Li, Li; Cui, Jianfang; Liu, Hong; Yang, Guodong

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VERSION 1 - REVIEW

Reviewer	**1**
Name	**Cakir, Selda Karaveli**
Affiliation	**Department of Nursing, Kastamonu University, School of Health Sciences, Kastamonu, Turkey.**
Date	**21-Feb-2025**
COI	**None**

Dear Author

Congratulations for your work.

I have a few small correction suggestions. I am sending in the attachment related to the reference writing Page 3 line 12 write the abbreviation for PEG

**** **The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.**

Reviewer	**2**
Name	**Esaki, Mitsuru**
Affiliation	**Kyushu University**
Date	**20-Mar-2025**

COI **None**

I am pleased to review the protocol of this interesting trial. This randomized controlled trial evaluates the efficacy and safety of combining linaclotide with oral sulfate solution for bowel preparation in chronic constipation patients undergoing colonoscopy, comparing three regimens: 2-day linaclotide with OSS, 3-day linaclotide with OSS, and OSS alone. The primary outcome is adequate bowel preparation defined by Boston Bowel Preparation Scale scores, with secondary outcomes including defecation frequency, cecal intubation rate, adenoma detection rate, and patient comfort. There are some comments on this protocol.

#1 The study compares three groups (2-day linaclotide+OSS, 3-day linaclotide+OSS, OSS alone), but the theoretical reasons for selecting these specific treatment durations should be more clearly explained. Particularly, a detailed explanation based on existing evidence is needed to justify the selection of 2-day versus 3-day linaclotide administration regimens.

#2. "In our center, the rate of adequate bowel preparation was 70% among chronic constipation patients." Please provide more detailed information about the baseline rate of 70% adequate bowel preparation, including the time period of data collection, patient characteristics, sample size, and whether this data was collected using identical preparation methods as the control arm (regimen C). This context is essential for evaluating the appropriateness of your sample size calculation and expected 20% difference between groups

#3. The statistical analysis section does not mention adjustment methods for multiple comparisons (e.g., Bonferroni correction) across the three study arms.

#4. The requirement for patients to discontinue laxatives and prokinetics seven days before colonoscopy represents a significant limitation of this study, as it restricts the eligible population to those who can tolerate a week without constipation medication, potentially limiting generalizability to the broader chronic constipation population.

#5. The protocol title contains "trail" which appears to be a typographical error for "trial."

#6. In the demographics data collection section, "body weight index (BMI)" is mentioned, which should be corrected to "body mass index (BMI)."

VERSION 1 - AUTHOR RESPONSE

Comments/suggestions from Reviewer #1

Comment: Congratulations for your work.I have a few small correction suggestions. I am sending in the attachment related to the reference writing Page 3 line 12 write the abbreviation for PEG (see attached marked up manuscript).

Response: We have corrected the abbreviation for PEG on Page 3 line 12, as suggested.

Comments/suggestions from Reviewer #2

Comment 1: The study compares three groups (2-day linaclotide+OSS, 3-day linaclotide+OSS, OSS alone), but the theoretical reasons for selecting these specific treatment durations should be more clearly explained. Particularly, a detailed explanation based on existing evidence is needed to justify the selection of 2-day versus 3-day linaclotide administration regimens.
Response1: We have added a detailed explanation for the selection of the 2-day and 3-day linaclotide administration regimens based on existing evidence. Considering the absence of prior studies on the combined use of linaclotide and OSS, our regimen is modeled on the combination use of linaclotide and PEG. Given that chronic constipation patients would experience first spontaneous bowel movements within 24 hours after taking linaclotide, and OSS is taken the day before and the day of the colonoscopy, we designed 2-day versus 3-day linaclotide administration regimens.
Comment 2: "In our center, the rate of adequate bowel preparation was 70% among chronic constipation patients." Please provide more detailed information about the baseline rate of 70% adequate bowel preparation, including the time period of data collection, patient characteristics, sample size, and whether this data was collected using identical preparation methods as the control arm (regimen C). This context is essential for evaluating the appropriateness of your sample size calculation and expected 20% difference between groups
Response 2: We have provided more detailed information about the baseline rate of 70% adequate bowel preparation, including the time period of data collection, patient characteristics, sample size and the methods used.
Comment 3: The statistical analysis section does not mention adjustment methods for multiple comparisons (e.g., Bonferroni correction) across the three study arms.
Response 3: We have included a description of the adjustment methods for multiple comparisons in the statistical analysis section.
Comment 4: The requirement for patients to discontinue laxatives and prokinetics seven days before colonoscopy represents a significant limitation of this study, as it restricts the eligible population to those who can tolerate a week without constipation medication, potentially limiting generalizability to the broader chronic constipation population.
Response 4: Though the requirement for patients to discontinue laxatives and prokinetics seven days before colonoscopy may restrict the eligible population to those who can tolerate a week without constipation medication. This could reflect the real impact of linaclotide in bowel preparation. This approach is also informed by prior research on bowel preparation in individuals with chronic constipation.
Comment 5: The protocol title contains "trail" which appears to be a typographical error for "trial."
Response 5: We have corrected the typographical error in the protocol title from ‘trail’ to ‘trial’.
Comment 6: In the demographics data collection section, "body weight index (BMI)" is mentioned, which should be corrected to "body mass index (BMI)."
Response 6: We have corrected the term ‘body weight index (BMI)’ to ‘body mass index (BMI)’ in the demographics data collection section.

VERSION 2 - REVIEW

Reviewer 1

Name Cakir, Selda Karaveli

Affiliation Department of Nursing, Kastamonu University, School of Health Sciences, Kastamonu, Turkey.

Date **10-Apr-2025**

COI

It seems that the suggested corrections have been made. thank you for your work