Clinical Trial/Experimental Study

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Antiemetics improve the tolerance of polyethylene glycol for colonoscopy preparation

A randomized clinical trial

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Abstract

Background: Bowel preparation is essential to the success of colonoscopy. However, many patients cannot finish the preparation due to nausea and vomiting when taking polyethylene glycol (PEG). Dopamine-2 receptor antagonists, such as domperidone and sulpiride, are classical antiemetic drugs. This study aimed to explore the effect of domperidone and sulpiride on reducing the discomforts associated with PEG.

Methods: Patients scheduled for colonoscopy were enrolled and randomly allocated into 3 groups. Patients in the domperidone group (Dom group) or sulpiride group (Sul group) took 2 doses of domperidone or sulpiride before PEG. Patients in the control group (Con group) followed the regular routine of PEG. Discomforts during bowel preparation and the quality of bowel preparation were assessed.

Results: A total of 306 patients were enrolled. The participants in the Dom group and Sul group completed PEG better and had fewer abdominal discomforts than those in the Con group. The severity of nausea and abdominal fullness was lower in the Dom group and Sul group. The quality of bowel preparation was better in the Dom group and Sul group than Con group.

Conclusions: Domperidone and sulpiride could reduce the PEG-related discomfort and improve the quality of bowel preparation. This method may be a promising way to improve the satisfaction of bowel preparation for both patients and endoscopists.

Abbreviations: 5-HT = 5-hydroxytryptamine, ANOVA = One-way Analysis of Variance, BBPS = Boston Bowel Preparation Scale, BMI = body mass index, CTZ = chemoreceptor trigger zone, ITT = intent-to-treat, PEG = polyethylene glycol, PP = per-protocol population.

Keywords: antiemetics, bowel preparation solutions, colonoscopy, polyethylene glycol

1. Introduction

Colonoscopy is widely used in the diagnosis and treatment of colorectal diseases. However, 10% to 20% of colonoscopies cannot be completed for various reasons, and inadequate bowel preparation is the most common one.[1] In addition, bowel preparation is essential to the diagnostic accuracy and operational safety of colonoscopy.[2,3] Therefore, improving the quality of bowel preparation is crucial to the success of colonoscopy.

Polyethylene glycol (PEG) is one of the most common laxatives used in bowel preparation before colonoscopy.[4] PEG is safe and effective and does not result in physiological or histological changes of the colon. It works most effectively when drank quickly (240 mL every 10 minutes).[4] However, 5% to 15% of patients cannot complete the preparation because of its poor taste and large volume.[5] A previous study reported that the inability to tolerate the full course of purgative was the most common barrier to optimal bowel preparation (in 78.7% of participants), and 72.5% of patients reported problems of palatability.[6] The most common side effects of PEG are nausea and vomiting.[4] Although various methods have been adopted to improve the adherence to bowel preparation, approximately 24% to 26% of patients complained of nausea or vomiting during bowel preparation in a Chinese population-based study.[7] Patients who failed the preparation because of severe vomiting are common in our hospital, and no efficient solution has been found.

Editor: Maorong Chen.

X-JY and PX contributed equally to this work.

National Natural Science Foundation of China (81970472, 81500412, 81970473, 81670484, 81470812, and 81270463); Pujiang Outstanding Youth Project of Renji Hospital South Campus, Grant/Award Number: RJPJYQ; 2018.

The authors have no conflicts of interest to disclose.

The datasets generated during and analyzed during the current study are available from the corresponding author on reasonable request.

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How to cite this article: Yan XJ, Xu P, Qiu HY, Wang B, Luo QQ, Chen SL. Antiemetics improve the tolerance of polyethylene glycol for colonoscopy preparation: A randomized clinical trial. Medicine 2021;100:10(e24947).

Received: 5 December 2020 / Received in final form: 3 February 2021 / Accepted: 7 February 2021

http://dx.doi.org/10.1097/MD.0000000000024947

Despite advances in prokinetic medicine, studies that aimed to explore possible drugs to reduce the discomforts during bowel preparation are inconsistent.[8] One investigation found that the frequencies of PEG-induced nausea and vomiting were not significantly changed after taking mosapride.[9] Another study found that mosapride and itopride could decrease the discomfort.[10] Thus, whether prokinetics are beneficial in the prevention of PEG-induced discomfort remains unknown. Dopamine-2 receptor antagonists, such as domperidone and sulpiride, are classical antiemetic drugs.[11,12] Domperidone has good efficacy in patients with functional dyspepsia.[13,14] Sulpiride is used to treat schizophrenia in high doses. Low doses of sulpiride have been proven to be safe and effective in treating nausea and vomiting.[15,16] However, it is unknown whether these antiemetics could prevent nausea and vomiting caused by bowel preparation. Therefore, this study was aimed to explore the effect of domperidone and sulpiride on discomfort associated with PEG.

2. Methods

2.1. Participants

This study was conducted according to the ethical principles of the Declaration of Helsinki and the requirements of local laws and regulations. Ethics approval was obtained from the Ethics Committee of Renji Hospital (Approval No: 2018-083). This trial was registered on ClinicalTrials.gov (NCT 04583111).

All patients who met the following criteria were introduced with the study, and those who agreed to participate were enrolled. The inclusion criteria were patients aged 18 to 80 years scheduled for colonoscopy. The exclusion criteria were intestinal obstruction or hemorrhage; allergy to domperidone, sulpiride or PEG; pregnancy or breastfeeding; previous use of antiemetics (including domperidone, sulpiride, metoclopramide, ondansetron, itopride, mosapride, etc) within 1 month; and previous bowel preparation within 3 months. Written informed consent was obtained from enrolled participants prior to the study.

2.2. Study design

This is a randomized, controlled, single-blind study. The enrolled patients were randomly allocated into 3 groups using a computer-generated random number list. All patients were restricted to take a low-residue diet the day before colonoscopy. A split-dose of 3L PEG was used for bowel preparation.[17,18] Thus, 1L of PEG was drank at 21:00 in the evening before the day of colonoscopy, and the remaining 2L was drank 4 to 6 hours before colonoscopy. Patients in the domperidone group (Dom group) took 2 doses of domperidone (10 mg) 30 minutes before the 2 doses of PEG.[11] Patients in the sulpiride group (Sul group) took 2 times of sulpiride (100 mg) 1 hour before the 2 doses of PEG.[16] Patients in the control group (Con group) followed the regular routine of 3L split-dose of PEG. Domperidone and sulpiride were explained to the participants as a supplement to bowel preparation. A telephone call about the instructions for bowel preparation was made the day before colonoscopy to guarantee the adherence of patients in all groups.

Demographic characteristics, such as age, gender, body mass index (BMI), constipation, and history of abdominal surgery were collected at entrance. Questionnaires about abdominal discomfort during bowel preparation were self-completed before colonoscopy. The quality of bowel preparation was assessed by 3 endoscopists during colonoscopy. The endoscopists were blind to the patient allocation.

2.3. Outcome measures

The primary endpoint of this study was the incidence of the discomfort during bowel preparation, including nausea, vomiting, abdominal fullness, and pain. These symptoms were assessed as none, mild, moderate, and severe. Patients with mild to severe symptoms were classified as having discomfort. The willingness to take PEG again was also recorded.

The secondary endpoint was the quality of bowel preparation assessed by the Boston Bowel Preparation Scale (BBPS) assessed during the withdrawal phase of colonoscopy.[19,20] The BBPS is the most thoroughly validated scale in analyzing the quality of bowel preparation.[19] The BBPS uses a 0 to 3 point scale assessing the bowel preparation quality in 3 segments of the colon (the right, transverse, and left colons). The 3 segment scores were then summed for a total score of 0 to 9, with 0 being unprepared and 9 being entirely clean.[20] BBPS scores ≥ 6 were defined as adequate bowel preparation.[19] For each participant, BBPS was assessed by 3 independent endoscopists, and the mean value was calculated. The compliance and adverse events of domperidone and sulpiride were also recorded.

2.4. Statistical analyses

Calculations of the treatment efficacy were based on the intent-to-treat population (ITT population, which included all enrolled subjects) and per-protocol population (PP population, which included patients who took at least 1 dose of domperidone or sulpiride). SPSS 22 software (IBM Corp., Armonk, New York) was used to conduct all statistical analyses. Normally distributed data is presented as the mean ± SD. One-way Analysis of Variance (ANOVA) was used to compare the differences among the 3 groups. Incidence among groups was analyzed with χ^2 test or Fisher's exact test. $P < .05$ was considered statistically significant.

The sample size calculation in this study was based on the assumption of a 20% difference in the incidence of discomfort between the Con group and the Dom or Sul group. The rate of discomfort during bowel preparation in our hospital was approximately 40%. To detect the difference with a significance level (α) of 0.05 and a power of 80% with a two-tailed test, at least 237 patients were needed. Approximately 5% of patients may cancel their colonoscopy in our center, thus we estimated that a total of 249 patients were needed for the study.

3. Results

3.1. Demographic and clinical characteristics of participants

A total of 306 patients were enrolled from March to September in 2020 and randomized into the Dom group (n = 102), Sul group (n = 102), or Con group (n = 102) (ITT population). Excluding patients who cancelled colonoscopy (3, 5, 4 participants in the 3 groups, respectively) or did not take antiemetics (13 participants did not take domperidone and 28 did not take sulpiride), 86, 69, and 98 participants were included in the 3 groups as PP population, respectively. A flowchart is shown in Figure 1. The

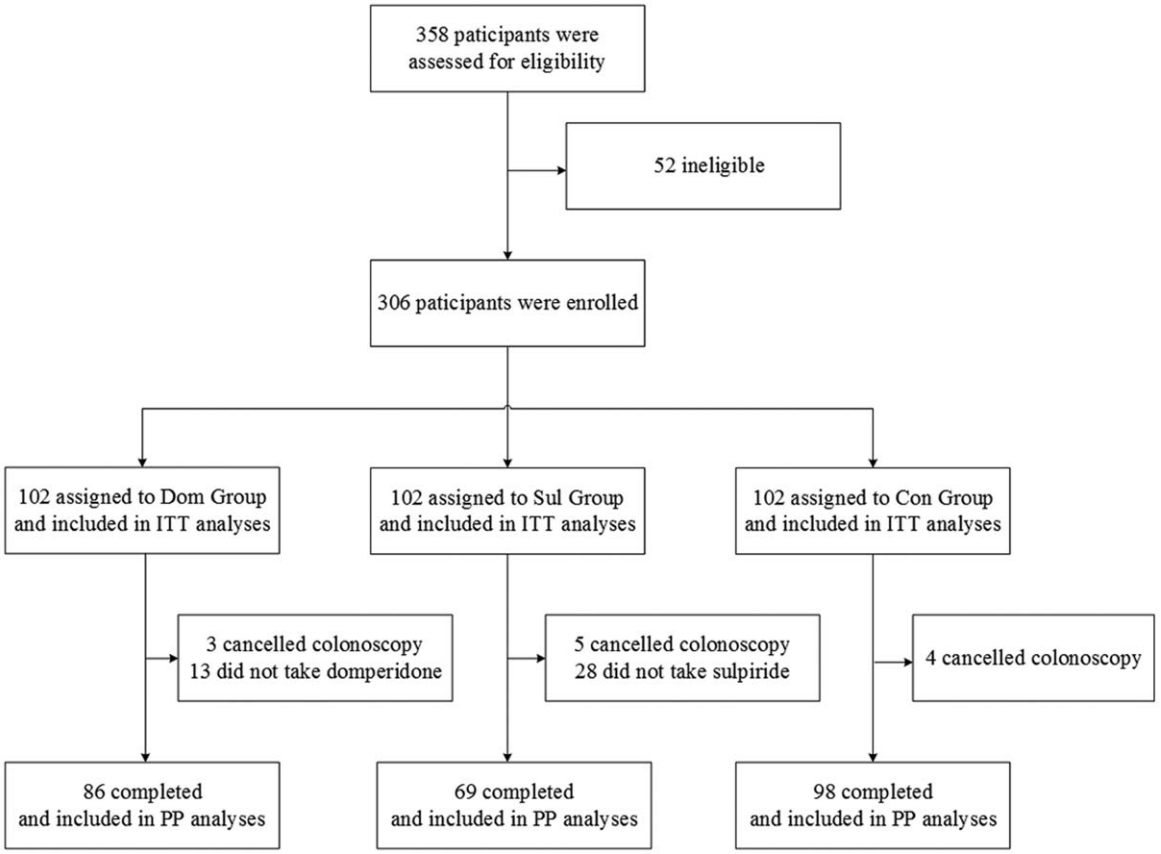

Figure 1. Flowchart of the enrolled patients.

demographic characteristics were well balanced among the 3 groups (ANOVA, Table 1).

3.2. Completion rate of PEG

The proportion of participants drinking 3L of PEG completely in the Dom group (97/102, 95.10%; $P=.084$ compared to Con group) and Sul group (94/102, 92.16%; $P=.356$ compared to Con group) was not statistically higher than that in the Con group (89/102, 87.25%, χ^2 test) based on the ITT population. In the PP population, the proportion of participants who finished drinking PEG in the Dom group (85/86, 98.84%; $P=.039$ compared to Con group) and Sul group (69/69, 100%; $P=.025$ compared to Con group) was significantly higher than that in the Con group (89/98, 90.82%; χ^2 test, Fig. 2).

3.3. Discomfort occurred during bowel preparation

The proportions of participants who complained of abdominal discomfort in the Dom group (21.57% *vs* 41.18%; $P<.01$) and Sul group (23.53% *vs* 41.18%; $P<.05$) were significantly lower than that in the Con group based on the ITT population (χ^2 test, Table 2). The severity of nausea and abdominal fullness in the Dom group and Sul group was lower than that in the Con group

Table 1

Demographic characteristics of the enrolled patients.

	Dom group (N=102)	Sul group (N=102)	Con group (N=102)
Age (yr)	49.71±12.24	52.68±12.51	50.68±12.83
Male:female	55:47	53:49	55:47
BMI	23.24±2.32	22.88±3.12	23.32±2.75
Constipation	12	13	12
History of abdominal surgery	26	25	27
Endoscopic findings			
Polyp	32	35	30
Inflammation	6	5	3
Cancer	1	2	1

Data of age and BMI are presented as the means±SD. BMI=body mass index.

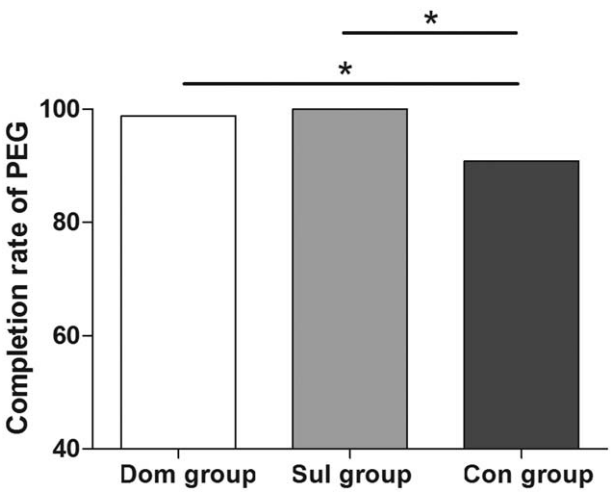

Figure 2. The completion rate of PEG based on the PP population. The proportion of participants who finished drinking PEG in the Dom group and Sul group was significantly higher than that in the Con group. $^{*}P < .05$ compared to the Con group; n = 86, 69, and 98 in the 3 groups, respectively; χ^2 test. PEG = polyethylene glycol; PP population = per-protocol population.

based on the PP population (nausea: $P < .01$ for Dom group *vs* Con group, $P < .05$ for Sul group *vs* Con group; abdominal fullness: $P < .05$ for Dom group *vs* Con group, $P < .01$ for Sul group *vs* Con group; n = 86, 69 and 98 in the 3 groups, respectively; Kruskal–Wallis test with post-test, Fig. 3). The severity of vomiting and abdominal pain was not significantly different among the 3 groups ($P > .05$; Kruskal–Wallis test with post-test, Fig. 3).

The percentage of participants who were willing to take PEG again was significantly higher in Dom group (88/102; $P < .01$ compared to Con group) and Sul group (85/102; $P < .01$ compared to Con group) than that in Con group (60/102; χ^2 test, Table 2).

3.4. The quality of bowel preparation

The mean BBPS scores were significantly higher in the Dom group than in the Con group based on the ITT population ($P < .01$ for Dom group *vs* Con group; $P > .05$ for Sul group *vs* Con group; n = 102; ANOVA with Tukey post-test, Fig. 4A). In the PP population, the mean BBPS scores were significantly higher in both the Dom group and Sul group than in the Con group (both $P < .01$ compared to Con group; n = 86, 69, and 98 in the 3 groups, respectively; ANOVA with Tukey post-test, Fig. 4B). In the ITT population, the percentage of patients who had adequate bowel preparation (BBPS scores ≥6) in Dom group was higher than that in Con group (85.29% *vs* 71.57%; $P = .027$, χ^2 test), while Sul group showed no statistical difference compared with Con group (78.43% *vs* 71.57%; $P = .332$; χ^2 test, Fig. 4C). In the PP population, the percentage of patients who had adequate bowel preparation in both Dom group (89.53% *vs* 74.49%; $P = .015$) and Sul group (89.86% *vs* 74.49%; $P = .022$) was higher than that in Con group (χ^2 test, Fig. 4D).

3.5. Safety analysis

Except for the discomforts associated with PEG analyzed above, no other adverse event occurred in any group.

4. Discussion

PEG-related nausea and vomiting are common in bowel preparation. In this study, we found for the first time that domperidone and sulpiride could increase the tolerance of bowel preparation and reduce the PEG-related discomfort.

We found that the groups of participants who took domperidone or sulpiride completed PEG better and had less discomfort, such as nausea and abdominal fullness. The antiemetic effect of domperidone depends on its activity at the chemoreceptor trigger zone (CTZ) outside the blood–brain barrier.[11] In addition, domperidone could accelerate gastric emptying by increasing the amplitude of esophageal motor function, enhancing antral contractions, and coordinating peristalsis across the pylorus.[11] Although the number of studies on the antiemetic properties of sulpiride is limited, low dose of sulpiride has been proven to be safe and effective in treating nausea and vomiting in clinical practice.[15,16,21] Sulpiride inhibits dopamine-2 receptors in CTZ and the gastrointestinal tract, which could inhibit vomiting by stimulating the motility of the upper gastrointestinal tract, accelerating gastric emptying, and increasing the resting tone of the gastroesophageal sphincter while producing relaxation of the pyloric sphincter.[16] In this study, we also found that the adherence of domperidone was better than that of sulpiride. It is possible that patients were more receptive to domperidone as a traditional antiemetic medicine. Some patients read the instruction of sulpiride and refused to take it as a "psychiatric medicine."

The incidence of discomforts in control group of this study (41.2%) is higher than a previous study conducted in Chinese

Table 2

The incidence of discomforts during bowel preparation based on the ITT population (N = 102 in each group).

	Dom group N (%)	Sul group N (%)	Con group N (%)
Nausea	17 (16.67)*	19 (18.63)*	33 (32.35)
Vomiting	11 (10.78)	10 (9.80)	18 (17.65)
Abdominal fullness	9 (8.82)*	8 (7.84)*	21 (20.59)
Abdominal pain	3 (2.94)	4 (3.92)	5 (4.90)
Patients with discomforts	22 (21.57)**	24 (23.53)*	42 (41.18)
Willing to take PEG again	88 (86.27)**	85 (83.33)**	60 (58.82)

PEG = polyethylene glycol.
$^{*}P < .05$.
$^{**}P < .01$ compared to the Con group, χ^2 test.

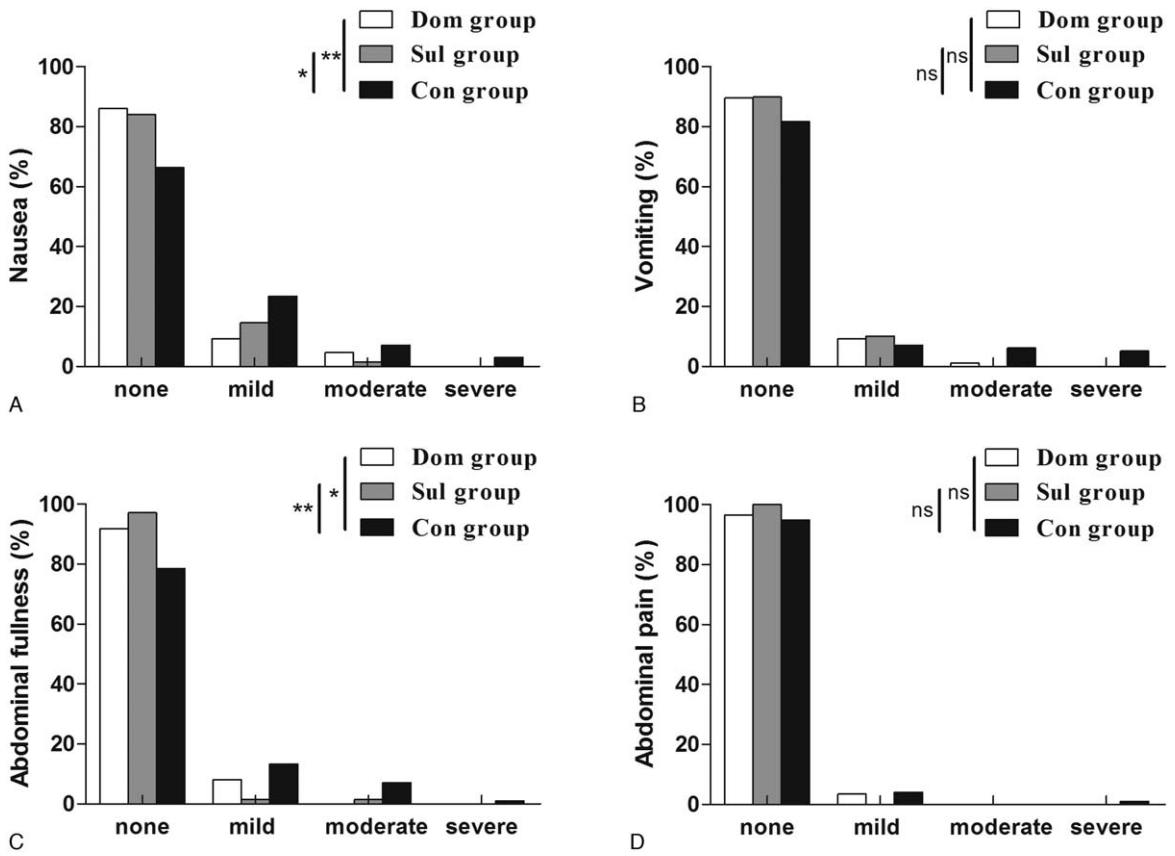

Figure 3. The severity of discomfort during bowel preparation based on the PP population. The severity of discomfort was assessed as none, mild, moderate, and severe during bowel preparation in each group. The severity of nausea (A) and abdominal fullness (C) in the Dom group and Sul group was significantly lower than that in the Con group. The severity of vomiting (B) and abdominal pain (D) was not significantly different among the 3 groups. $^{*}P < .05$, $^{**}P < .01$ compared to Con group; n = 86, 69, and 98 in the 3 groups, respectively; Kruskal–Wallis test with post-test. PP population = per-protocol population.

population (26.7%).[7] It is possible that patients were more likely to report the discomfort as they were informed that this study is aimed to assess the discomforts associated with PEG.

Other antiemetics were explored to prevent PEG-induced discomforts in previous studies. Two studies on metoclopramide, another dopamine-2 receptor antagonist with 5-hydroxytryptamine (5-HT3) receptor antagonist and 5-HT4 receptor agonist properties, were controversial.[22,23] Although there is no literature comparing the antiemetic efficacy of domperidone, sulpiride and metoclopramide, 1 study on functional dyspepsia found that the effect of sulpiride was significantly better than domperidone and metoclopramide.[24] Itopride acts as both a dopamine-2 antagonist and cholinesterase inhibitor.[25] It has been reported that itopride could decrease the discomforts associated with PEG.[10] Except for dopamine-2 receptor antagonists, other studies have explored the effect of mosapride on PEG-induced discomforts, and the results were conflicting.[9,10,26] Mosapride facilitates acetylcholine release from the enteric cholinergic neurons by its selective 5-HT4 receptor agonistic action in the stomach and colon.[27] Although the antiemetic effect of mosapride has not been proven at present, 1 study reported that a single administration of mosapride can enhance gastric accommodation in humans.[28] More researches are needed to clarify the effects of various antiemetics on PEG-related discomforts.

Other methods to reduce nausea caused by PEG have been explored in previous studies. One study based on ambulatory patients found that orange juice could reduce nausea caused by PEG.[29] However, using Coke or pineapple juice as a solvent failed to reduce the discomforts associated with PEG.[30,31] Two studies proved that gum chewing was efficient in decreasing nausea or increasing satisfaction.[32,33]

Our study showed that the quality of bowel preparation was also increased in the Dom group and Sul group. As domperidone and sulpiride are mainly bound to tissues on the esophagus, stomach, and small intestine,[11,16] we presume that this benefit was also based on the increased tolerance of PEG rather than accelerated motility of the colon.

Domperidone is suggested to be prescribed at doses of 30 to 80 mg daily to prevent side effects such as QT prolongation and sudden cardiac death.[34] In this study, no side effect was reported with low dose of domperidone (20 mg). The limitation of this study is the absence of placebo in the control group. Therefore, we could not rule out the placebo effect.

In conclusion, domperidone and sulpiride are effective and safe in increasing the tolerance of PEG and quality of bowel preparation. This method may be a promising way to improve the satisfaction of bowel preparation for both patients and endoscopists.

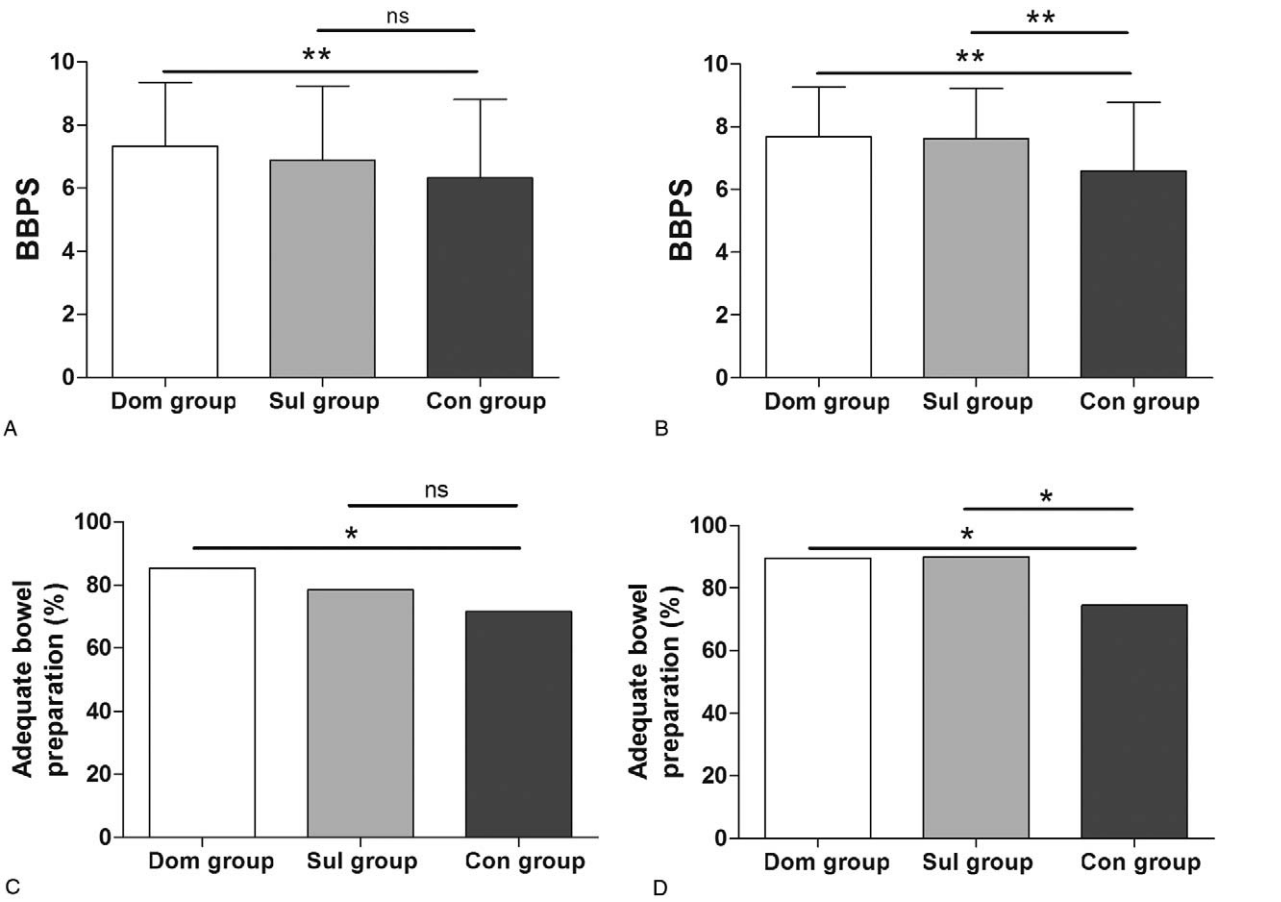

Figure 4. The quality of bowel preparation. (A) BBPS scores in each group based on the ITT population. (B) BBPS scores based on the PP population. $^{**}P < .01$ compared to the Con group, ANOVA with Turkey post-test. (C) The percentage of patients who had adequate bowel preparation (BBPS scores ≥ 6) based on the ITT population. (D) The percentage of patients who had adequate bowel preparation based on the PP population. $^{*}P < .05$ compared to the Con group, χ^2 test. BBPS = Boston Bowel Preparation Scale; ITT population = intent-to-treat population; PP population = per-protocol population.

Author contributions

HYQ and BW recruited and allocated participants; SLC, PX, and QQL performed colonoscopy; XJY analyzed data; XJY and PX prepared manuscript; SLC designed study and reviewed the manuscript.

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Data curation: Xiu-Juan Yan.
Project administration: Ping Xu, Hong-Yi Qiu, Bo Wang, Qing-Qing Luo.
Writing – original draft: Xiu-Juan Yan, Ping Xu.
Writing – review & editing: Sheng-Liang Chen.

References

[1] Mitchell RM, McCallion K, Gardiner KR, et al. Successful colonoscopy; completion rates and reasons for incompletion. Ulster Med J 2002;71:34–7.
[2] Rex DK, Petrini JL, Baron TH, et al. Quality indicators for colonoscopy. Am J Gastroenterol 2006;101:873–85.
[3] Mathus-Vliegen E, Pellisé M, Heresbach D, et al. Consensus guidelines for the use of bowel preparation prior to colonic diagnostic procedures: colonoscopy and small bowel video capsule endoscopy. Curr Med Res Opin 2013;29:931–45.
[4] Saltzman JR, Cash BD, Pasha SF, et al. Bowel preparation before colonoscopy. Gastrointest Endosc 2015;81:781–94.
[5] Marshall JB, Pineda JJ, Barthel JS, et al. Prospective, randomized trial comparing sodium phosphate solution with polyethylene glycol-electrolyte lavage for colonoscopy preparation. Gastrointest Endosc 1993; 39:631–4.
[6] Hillyer GC, Basch CH, Basch CE, et al. Gastroenterologists' perceived barriers to optimal pre-colonoscopy bowel preparation: results of a national survey. J Cancer Educ 2012;27:526–32.
[7] Liu X, Luo H, Zhang L, et al. Telephone-based re-education on the day before colonoscopy improves the quality of bowel preparation and the polyp detection rate: a prospective, colonoscopist-blinded, randomised, controlled study. Gut 2014;63:125–30.
[8] Hassan C, East J, Radaelli F, et al. Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Guideline – update 2019. Endoscopy 2019;51:775–94.
[9] Tajika M, Niwa Y, Bhatia V, et al. Efficacy of mosapride citrate with polyethylene glycol solution for colonoscopy preparation. World J Gastroenterol 2012;18:2517–25.
[10] Mishima Y, Amano Y, Okita K, et al. Efficacy of prokinetic agents in improving bowel preparation for colonoscopy. Digestion 2008;77:166–72.
[11] Reddymasu SC, Soykan I, McCallum RW. Domperidone: review of pharmacology and clinical applications in gastroenterology. Am J Gastroenterol 2007;102:2036–45.
[12] Gallego D, Ortega O, Arenas C, et al. The effect of levosulpiride on in vitro motor patterns in the human gastric fundus, antrum, and jejunum. Neurogastroenterol Motil 2016;28:879–90.
[13] Yang YJ, Bang CS, Baik GH, et al. Prokinetics for the treatment of functional dyspepsia: Bayesian network meta-analysis. BMC Gastroenterol 2017;17:83.

[14] Pittayanon R, Yuan Y, Bollegala NP, et al. Prokinetics for functional dyspepsia. Cochrane Database Syst Rev 2018;10:Cd009431.
[15] Luo L, Du L, Shen J, et al. Benefit of small dose antidepressants for functional dyspepsia: experience from a tertiary center in eastern China. Medicine (Baltimore) 2019;98:e17501.
[16] Cohen N, Alon I, Almoznino-Sarfian D, et al. Sulpiride versus metoclopramide in nononcologic patients with vomiting or nausea. J Clin Gastroenterol 1999;29:59–62.
[17] Zhang S, Li M, Zhao Y, et al. 3-L split-dose is superior to 2-L polyethylene glycol in bowel cleansing in Chinese population: a multicenter randomized, controlled trial. Medicine (Baltimore) 2015; 94:e472.
[18] Chinese guideline for bowel preparation for colonoscopy (2019, Shanghai). Zhonghua Nei Ke Za Zhi 2019;58:485–95.
[19] Kaminski MF, Thomas-Gibson S, Bugajski M, et al. Performance measures for lower gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative. Endoscopy 2017;49:378–97.
[20] Calderwood AH, Jacobson BC. Comprehensive validation of the Boston Bowel Preparation Scale. Gastrointest Endosc 2010;72:686–92.
[21] Mansi C, Borro P, Giacomini M, et al. Comparative effects of levosulpiride and cisapride on gastric emptying and symptoms in patients with functional dyspepsia and gastroparesis. Aliment Pharmacol Ther 2000;14:561–9.
[22] Brady CE3rd, DiPalma JA, Pierson WP. Golytely lavage – is metoclopramide necessary? Am J Gastroenterol 1985;80:180–4.
[23] Rhodes JB, Engstrom J, Stone KF. Metoclopramide reduces the distress associated with colon cleansing by an oral electrolyte overload. Gastrointest Endosc 1978;24:162–3.
[24] Singh H, Bala R, Kaur K. Efficacy and tolerability of levosulipride, domperidone and metoclopramide in patients with non-ulcer functional dyspepsia: a comparative analysis. J Clin Diagn Res 2015;9:Fc09–12.
[25] Van den Houte K, Carbone F, Pauwels A, et al. Influence of itopride and domperidone on gastric tone and on the perception of gastric distention in healthy subjects. Neurogastroenterol Motil 2019;31:e13544.
[26] Lee J, Jeong SJ, Kim TH, et al. Efficacy of mosapride citrate with a split dose of polyethylene glycol plus ascorbic acid for bowel preparation in elderly patients: a randomized controlled trial. Medicine (Baltimore) 2020;99:e18702.
[27] Taniyama K, Makimoto N, Furuichi A, et al. Functions of peripheral 5-hydroxytryptamine receptors, especially 5-hydroxytryptamine4 receptor, in gastrointestinal motility. J Gastroenterol 2000;35:575–82.
[28] Amano T, Ariga H, Kurematsu A, et al. Effect of 5-hydroxytryptamine receptor 4 agonist mosapride on human gastric accommodation. Neurogastroenterol Motil 2015;27:1303–9.
[29] Choi HS, Shim CS, Kim GW, et al. Orange juice intake reduces patient discomfort and is effective for bowel cleansing with polyethylene glycol during bowel preparation. Dis Colon Rectum 2014;57:1220–7.
[30] Altınbas A, Aktas B, Yılmaz B, et al. Adding pineapple juice to a polyethylene glycol-based bowel cleansing regime improved the quality of colon cleaning. Ann Nutr Metab 2013;63:83–7.
[31] Seow-En I, Seow-Choen F. A prospective randomized trial on the use of Coca-Cola Zero(®) vs water for polyethylene glycol bowel preparation before colonoscopy. Colorectal Dis 2016;18:717–23.
[32] Lee J, Lee E, Kim Y, et al. Effects of gum chewing on abdominal discomfort, nausea, vomiting and intake adherence to polyethylene glycol solution of patients in colonoscopy preparation. J Clin Nurs 2016;25:518–25.
[33] Fang J, Wang SL, Fu HY, et al. Impact of gum chewing on the quality of bowel preparation for colonoscopy: an endoscopist-blinded, randomized controlled trial. Gastrointest Endosc 2017;86:187–91.
[34] Field J, Wasilewski M, Bhuta R, et al. Effect of chronic domperidone use on QT interval: a large single center study. J Clin Gastroenterol 2019;53:648–52.