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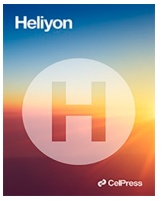

Research article

Vitamin drinks improve palatability and reduce adverse events associated to polyethylene glycol electrolyte solutions

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A R T I C L E I N F O

Keywords:
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A B S T R A C T

Background: The unpleasant taste of polyethylene glycol (PEG) has been a hindrance to patients undergoing colonoscopy.

Aim: This study aims to determine whether the addition of a vitamin drink (Mizone) to the 4L split-dose PEG regimen would be effective in improving the solution's palatability, and reducing patient discomfort during bowel preparation.

Methods: The present prospective, single endoscopist-blinded, randomized controlled study randomly assigned patients into two groups: PEG + Mizone group (3.6 L of PEG solution plus 0.4 L of Mizone) and PEG group (4 L of PEG solution). Palatability was assessed using a Likert scale of 1–5. The adverse events, amount of unconsumed solution, and willingness to repeat the same process were recorded through a questionnaire. The present study was registered in the Chinese Clinical Trial Registry (ChiCTR2000034484).

Results: A total of 132 patients were included. The demographic characteristics of these patients were comparable between the two groups. The palatability score (mean ± standard deviation [SD]) was higher in the PEG + Mizone group, when compared to the control group (4.00 ± 0.859 *vs.* 2.95 ± 0.999, $p < 0.001$). Furthermore, the incidence of nausea was lower in the PEG + Mizone group (9.1 % *vs.* 28.8 %, $p = 0.004$), while the other adverse events were similar between the two groups. The percentage of the completely consumed pre-prepared solution was significantly greater in the PEG + Mizone group (95.5 % *vs.* 78.8 %, $p = 0.004$). Furthermore, the willingness to repeat the same process was higher in the PEG + Mizone group (83.3 % *vs.* 42.4 %, $p < 0.001$). However, the consumption of either of these preparations did not significantly affect the electrolyte and blood glucose levels, and renal function.

Conclusion: Compared to the conventional 4L PEG bowel preparation, the use of a vitamin drink (Mizone) as an adjuvant can improve the palatability, reduce adverse events, and increase the patient's willingness to undergo bowel preparation with the same regimen.

1. Introduction

Colonoscopy is presently the gold standard for screening and diagnosing colorectal disease. Furthermore, this can reveal the nature of the lesion through pathological biopsy. Colorectal cancer morbidity and mortality can be reduced by removing precancerous lesions,

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and cancer can be detected at an earlier, more treatable stage [1,2]. Adequate bowel preparation prior to colonoscopy is a prerequisite for the safe and effective application of colonoscopy [3]. Unqualified bowel preparation may affect mucosal observation, surgical completion, and missed lesions during colonoscopy, resulting in a shortened colonoscopy cycle. This would greatly increase the economic burden on patients, reduce the benefits of colonoscopy, and result in waste of medical resources [4].

The polyethylene glycol (PEG) electrolyte solution is the most commonly used colonic cleansing agent and laxative in various institutions. Since its aqueous solution is isotonic, this does not cause significant water or electrolyte changes. However, ingestion of a large amount of water is required to wash the intestines [5]. Studies have revealed that the 4L split-dose PEG regimen can provide better bowel preparation quality, when compared to other regimens, especially in the right colon, and that the compliance for the 4L split-dose PEG regimen was significantly better, when compared to that of a single-dose regimen, with relatively few adverse events. Thus, this has been regarded as the standard bowel preparation regimen [6–8]. However, the unpleasant bitter taste and large volume required for proper cleansing are the most frequently reported reasons for avoiding colonoscopy [9]. As a result, this formulation has been poorly tolerated by patients. This has resulted in incomplete compliance, and the inability to complete the recommended dose, leading to low-quality bowel preparation.

Previous studies have revealed that adding Gatorade to a low dose of PEG was associated to greater satisfaction in patients' overall experience. However, this was not as effective as the 4L split-dose PEG in bowel cleansing [10]. In a recent study, a 3L PEG intestinal preparation solution that consisted of 1.2 L of water and 1.8 L of Mizone fluid was shown to reduce the occurrence of bloating in patients. However, some patients felt that the taste of the solution was too sweet, and it was unclear whether the addition of Mizone had any effect on the patient's serum electrolyte levels [11]. At present, merely one trial has explored the potential effect of Mizone on bowel preparations through the combined application of PEG. Mizone, which is a first brand power index, is a popular low-sugar vitamin drink in China. This is rich in vitamin C, vitamin B6, and vitamin B12, and the taste of Mizone is sweet and sour, which is liked by a number of people. Therefore, we hypothesized that reducing the percentage of Mizone can further improve the palatability of the PEG solution. The present study aimed to explore the optimal ratio of Mizone to water, in order to improve its palatability. Furthermore, the effectiveness and safety of PEG combined with Mizone in bowel preparation was investigated.

2. Materials and methods

2.1. Study design

The present prospective, single-center, single blinded, randomized clinical trial adhered to the tenets of the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of The Affiliated Changzhou No. 2 People's Hospital of Nanjing Medical University on November 27, 2019 ([2019] KY042-01). Furthermore, the present study was registered in the Chinese Clinical Trial Registry on July 6, 2020 (ChiCTR2000034484). A written informed consent was obtained from all individual participants included in the study.

2.2. Study subjects and randomization

The present study was conducted in the Affiliated Changzhou No. 2 People's Hospital of Nanjing Medical University from June 2021 to December 2021. Outpatients and inpatients within 18–80 years old, who were scheduled to undergo colonoscopy for routine screening and surveillance, were consecutively enrolled for the present study. The following exclusion criteria were used: (1) severe cardiovascular, hepatic, renal, or hematopoietic failure; (2) bowel obstruction or perforation; (3) significant gastroparesis or gastric outlet obstruction; (4) toxic megacolon or severe inflammatory bowel disease; (5) pregnant or lactating women; (6) previous allergy to PEG or vitamin drinks; (7) patients with significant electrolyte anomalies; (8) patients with diabetes. Eligible patients were randomized into two groups for bowel preparation at a 1:1 ratio by a research coordinator using a randomization list generated from the Statistical Package for Social Sciences for Windows version 26.0 (IBM Corp., Armonk, NY, USA). Initially, numbers 001–132 were assigned to 132 patients, and a random number seed (202007) was set to ensure the reproducibility of the output data. Then, the Rv. Uniform (0, 1) function was used to generate a random number between (0, 1) for each record. Finally, the study subjects were randomly divided into different groups using the block randomization method, with a block size of 2. Patients with smaller random numbers in each block were included in the experimental group, while patients with larger random numbers were included in the control group. The investigators did not have access to the randomization list, and the randomized bowel preparation was stored in the medical record that was not accessible to the endoscopist. The experimental group received PEG + Mizone and the control group received PEG alone. The colonoscopies were performed by a single experienced endoscopist, who was blinded to the group allocation, using a high-definition video colonoscope (CF- HQ290 video colonoscope; Olympus Co., Tokyo, Japan).

The endoscopist that performed the colonoscopy was blinded to the patient name, and was not allowed to interact with patients on drug-related activities before or during the procedures, in order to ensure the maintenance of blinding. The patients were instructed not to reveal their bowel preparation to the endoscopist.

2.3. Study materials

The PEG powder (Fu Jingqing, Beaufour Ipsen Pharmaceutical Co. Ltd.) was packed into a box that included four bags of the same reagent. Each bag of reagent consisted of the following reagents: 64 g of PEG4000, 5.7 g of anhydrous sodium sulfate, 1.68 g of sodium bicarbonate, 1.460 g of sodium chloride, and 0.75 g of potassium chloride. Mizone (lime flavor; Danone China Food & Beverage) was

used for the present study. Each 100-mL bottle contained 20 mg of vitamin C, 0.8 mg of nicotinamide, 0.09 mg of vitamin B6, 0.1 μg of vitamin B12, and 4.8 g of sugar. A total of four bags of PEG powder and 4 L of clear water were used to produce the 4L PEG solution, while a total of four bags of PEG powder with 3.6 L of clear water and 0.4 L of Mizone were used to produce the 4L PEG-Mizone solution.

2.4. Bowel preparation

At the scheduled time, the patients received verbal instructions and a typed instruction sheet for the preparation steps. Patients in the PEG + Mizone group were provided with a free bottle of Mizone (lime flavor, 0.4 L). All patients were instructed to adhere to a 1-day low-fiber diet before the colonoscopy [12]. Furthermore, these patients were instructed to have dinner before 6 p.m. Patients in the PEG + Mizone group (experimental group) received 3.6 L of PEG solution plus 0.4 L of Mizone, while patients in the PEG group (control group) received 4 L of PEG solution for bowel preparation. These patients were instructed to ingest 2 L of the solution between 7 and 9 p.m. on the day before the colonoscopy. Then, a 2-L dose was required to be completed in the morning, at a minimum of 4 h, but no later than 6 h, before the procedure. All patients orally received simethicone (30 mL, 1200 mg; Berlin-Chemie AG, Berlin, Germany) after ingestion of the PEG solution [13].

2.5. Data collection

These patients were instructed to complete a questionnaire that was used in similar previous studies [14,15] to collect the following information: the total amount of bowel preparation solution consumed, the time of solution ingestion, palatability, willingness to repeat the same bowel preparation, and related adverse events before the colonoscopy. Palatability was assessed using a Likert scale of 1–5 (very poor, poor, neutral, good, and very good) [11]. Adverse events (nausea, vomiting, bloating, abdominal pain, sleep disturbance, and headache) related to bowel preparation were reported by the patients. The Boston bowel preparation scale (BBPS) score was used to rate the cleanliness of the three segments of the colon (ascending, transverse, and descending colon) on a scale of 0–3 [16]. The individual segment scores were added up, and the total bowel cleansing scores ranged from 0 (very poor) to 9 (excellent). In the present study, a total BBPS score of $\geq$6 and a score of $\geq$2 per segment were considered as adequate bowel preparation [17]. Serum blood measurements to determine the concentration of sodium, potassium, chloride, blood glucose, bicarbonate, urea, and creatinine were performed at the first clinic visit prior to bowel preparation, and these were repeated before the colonoscopy was performed.

2.6. Sample size calculation and statistical analysis

The sample size was calculated based on the volunteers that assessed the taste of PEG with Mizone in different proportions. A total of 45 blinded healthy subjects were recruited and divided into different groups (pure water, Mizone and water at 1:1, Mizone and water at 1:5, Mizone and water at 1:9, and pure Mizone, with nine people in each group). Each participant was given 100 ml of pre-prepared bowel cleansing solution to rate its palatability using a Likert Visual Scale with a range of 1–5. The average palatability score for each group was 3.670 ± 1.000, 3.890 ± 0.782, 4.000 ± 0.500, 4.220 ± 0.972, and 3.110 ± 0.782, respectively. Therefore, the

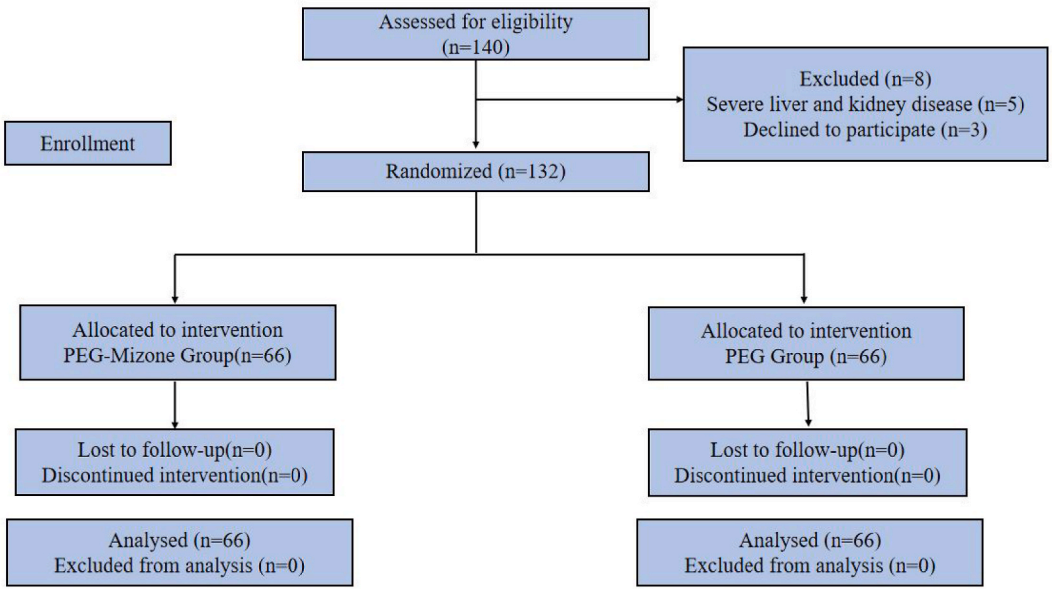

Fig. 1. Flowchart for the patient recruitment and randomization. PEG, polyethylene glycol.

Mizone-to-water ratio was modulated at a ratio of 1:9 for the PEG solution, and this was assigned to the PEG + Mizone group (experimental group). The average palatability score in the PEG group and PEG + Mizone group was 3.670 ± 1.000 and 4.220 ± 0.972 points, respectively. Based on these palatability scores, and using an α value of 0.05 and a power of 0.80, the sample size required to attain significance, as calculated by the PASS 15.0 software, was 52 people per group. Considering a drop rate of 20 %, the required sample size was 65. All continuous variables followed a normal distribution. Continuous variables were presented as mean ± standard deviation (SD), and these were compared between the two groups by independent samples *t*-test. Categorical variables were presented as percentage, and these were compared using Pearson's X^2-test or Fisher's precision probability test. The Statistical Package for Social Sciences for Windows version 26.0 (IBM Corp., Armonk, NY, USA) was used for the data entry and statistical analysis. A p-value <0.05 was considered statistically significant.

3. Results

3.1. Patient characteristics

A total of 140 adult patients were screened for eligibility in the present study (Fig. 1). Eight patients did not meet the inclusion criteria due to severe liver and kidney disease ($n = 5$), and refusal to participate ($n = 3$). The remaining 132 patients were enrolled for analysis in the present study, which included 66 patients in the PEG + Mizone group and 66 patients in the PEG group. There were no statistically significant differences between the two groups, in terms of baseline characteristics, which included gender, age, height, body weight, smoking, drinking, education level, abdominal surgery, comorbidities, timing of colonoscopy, and constipation. The number of patients with first-time colonoscopy, and the percentage of outpatients were similar in both groups (Table 1).

3.2. Palatability and acceptability

The time of solution ingestion was not different between the PEG + Mizone group and PEG group (231.82 ± 26.48 min *vs.* 229.06 ± 35.41 min, $p = 0.613$). The palatability score (mean ± SD) was higher in the PEG + Mizone group, when compared to the control group (4.000 ± 0.859 *vs.* 2.950 ± 0.999, $p < 0.001$). Furthermore, the palatability score was also higher in the PEG + Mizone group (which comprised of patients who had first-time colonoscopy), when compared to the control group (4.070 ± 0.745 *vs.* 3.020 ± 1.010, $p < 0.001$). Moreover, the proportion of patients who drank the entire bowel preparation solution was significantly higher in the PEG + Mizone group (95.5 % *vs.* 78.8 %, $p = 0.004$). In addition, patients in the PEG + Mizone group had a higher willingness to repeat the same process if they needed a secondary colonic preparation (83.3 % *vs.* 42.4 %, $p < 0.001$) (Table 2).

3.3. Endoscopic findings and quality of bowel cleansing

The overall endoscopic findings, which included the polyp detection rate (27.3 % *vs.* 24.2 %), were not statistically different between the two groups. Furthermore, the cecal intubation rates did not significantly differ between the two groups. The colonoscopic data is presented in Table 3. The rate of adequate bowel preparation (BBPS ≥6) was similar in both groups (93.9 % *vs.* 87.9 %, $p = 0.226$). The bowel cleansing effect obtained according to the BBPS score is presented in Table 4. The total BBPS score in the PEG + Mizone group was similar to that in the PEG group (6.41 ± 1.34 *vs.* 6.38 ± 1.29, $p = 0.895$). Furthermore, the BBPS scores for the right,

Table 1
Baseline characteristics of the study subjects.

	PEG + Mizone group ($n = 66$)	PEG group ($n = 66$)	p
Age (years, mean ± SD)	47.60 ± 12.90	50.00 ± 13.20	0.281
Male gender, *n* (%)	34 (51.50)	30 (45.50)	0.486
Height (cm, mean ± SD)	164.90 ± 8.00	165.90 ± 8.40	0.498
Weight (kg, mean ± SD)	63.40 ± 11.10	65.50 ± 14.10	0.335
BMI (kg/m^2, mean ± SD)	23.20 ± 2.90	23.70 ± 3.80	0.446
Smoking, *n* (%)	11 (16.70)	11 (16.70)	1.000
Drinking, *n* (%)	10 (15.20)	11 (16.70)	0.812
Education level, *n* (%)			0.069
Elementary school	5 (7.60)	12 (18.20)	
High School and University	61 (92.40)	54 (81.80)	
Comorbidities			
Hypertension	19 (28.80)	15 (22.70)	0.426
Coronary heart disease	0 (0.00)	1 (1.50)	1.000
History of abdominal surgery, *n* (%)	18 (27.30)	18 (27.30)	1.000
Outpatients: Inpatients	46:20 (69.70)	43:23 (65.20)	0.577
Timing of colonoscopy, *n* (%)			0.434
Morning	46 (69.70)	50 (75.80)	
Afternoon	20 (30.30)	16 (24.20)	
First-time colonoscopy, *n* (%)	42 (63.60)	51 (77.30)	0.086
Constipation, *n* (%)	4 (6.10)	3 (4.50)	1.000

Notes: PEG, polyethylene glycol; SD, standard deviation; BMI, body mass index.

Table 2
Palatability and tolerability of the bowel preparations.

	PEG + Mizone group($n = 66$)	PEG group($n = 66$)	p
Palatability score, mean ± SD	4.00 ± 0.859	2.950 ± 0.999	<0.001
1. Very poor	0 (0.00)	4 (6.10)	
2. Poor	4 (6.10)	20 (30.30)	
3. Neutral	12 (18.20)	19 (28.80)	
4. Good	30 (45.50)	21 (31.80)	
5. Very good	20 (30.30)	2 (3.00)	
Complete intake			0.004
100 %	63 (95.50)	53 (78.80)	
≥50 %	3 (4.50)	13 (19.70)	
<50 %	0 (0.00)	1 (1.50)	
Willingness to repeat the process, *n* (%)			<0.001
Yes	55 (83.30)	28 (42.40)	
No	11 (16.70)	38 (57.60)	
Time of solution ingestion (min)	231.82 ± 26.48	229.06 ± 35.41	0.613

Notes: PEG, polyethylene glycol; SD, standard deviation.

transverse, and left colon were not different between the two groups (Table 4).

3.4. Adverse events and safety

The incidence of nausea was lower in the PEG + Mizone group, when compared to the PEG group (9.1 % *vs.* 28.8 %, $p = 0.004$). The incidence of vomiting was lower in the PEG + Mizone group, when compared to the PEG group (1.5 % *vs.* 10.6 %, $p = 0.068$), although there was no statistical significance. The incidences of other adverse events were similar between the two groups (Table 5). For the 23 patients, blood samples were taken before and after bowel preparation (11 patients from the PEG + Mizone group and 12 patients from the PEG group). There were no significant differences in blood glucose, renal function, and serum electrolytes before and after bowel preparation (Table 6).

4. Discussion

Colorectal cancer is the third most common cancer in the world, and its mortality rate ranks second in the world [18]. Colonoscopy screening can reduce the incidence and mortality of colorectal cancer. However, a number of patients consider preoperative bowel preparation as the most worrisome aspect of colonoscopy [19,20], and poor palatability remains as a major challenge in taking the laxative [21]. In the present study, Mizone was used as an adjuvant to investigate its benefit in a high-volume 4L split-dose PEG regimen. It was found that the addition of Mizone significantly improved the palatability of the PEG regimen. Furthermore, most patients (95.6 %) in the PEG + Mizone group were able to ingest the entire 4L of PEG, and were willing to repeat the procedure. This result was similar to that reported by previous trials that used Orange Juice or Sugar-free menthol candy, in conjunction to the PEG solution [22,23]. In terms of adverse events, the addition of Mizone appears to be more effective in reducing nausea and vomiting. The potential explanations underlying this phenomenon may be, as follows: Mizone has a delicious sweet and sour flavor, which dilutes the special bitter taste of the PEG solution. In addition, the improvement in palatability was associated to increased appetite [24], leading to the faster intake of the PEG solution, and low experience of nausea and vomiting. The effect of palatability is through the stimulation of positive feedback mechanisms to counteract the negative feedback mechanisms associated to satiety [25,26]. Lastly, Mizone is rich in vitamins, especially vitamin C and vitamin B6. Vitamin C has a laxative effect. Once the absorption of high-concentration vitamin C in the intestine reaches saturation (the daily intake is more than 1 g), the rest remains in the intestinal cavity, acting synergistically with PEG as an osmotic laxative [27,28]. Some studies [29,30] have reported that compared to the sole use of PEG, the addition of vitamin C can increase patient acceptance, and reduce adverse reactions, such as nausea and vomiting. Vitamin B6 supplementation can significantly improve hyperemesis gravidarum, and reduce nausea in pregnant women [31].

Considering the effectiveness of the bowel preparation, there was no difference in total BBPS scores, although there was a difference in the total amount of bowel preparation solution consumed. The present study adopted the split-dose regimen for bowel preparations, with a short time interval between the bowel preparation education and colonoscopy [32,33]. These may be the possible explanations.

Table 3
Comparison of colonoscopy findings between the two groups.

	PEG + Mizone group ($n = 66$)	PEG group ($n = 66$)	p
Polyp, *n* (%)	18 (27.30)	16 (24.20)	0.691
Colorectal cancer, *n* (%)	1 (1.50)	2 (3.00)	1.000
Diverticulosis, *n* (%)	2 (3.00)	0 (0.00)	0.476
Melanosis coli, *n* (%)	1 (1.50)	1 (1.50)	1.000
Cecal intubation rate, (%)	100	100	1.000

Notes: PEG, polyethylene glycol.

Table 4
Quality of bowel cleansing according to the Boston bowel preparation scale in both groups.

	PEG + Mizone group ($n = 66$)	PEG group ($n = 66$)	p
Boston score, mean ± SD	6.41 ± 1.34	6.38 ± 1.29	0.895
Right colon	2.08 ± 0.47	2.08 ± 0.54	1.000
Transverse colon	2.20 ± 0.53	2.18 ± 0.52	0.868
Left colon	2.22 ± 0.45	2.24 ± 0.46	0.869
Adequate bowel preparation, ≥6, *n* (%)	62 (93.90)	58 (87.90)	0.226

Notes: PEG, polyethylene glycol; SD, Standard deviation.

Table 5
Adverse events reported by the study participants.

	PEG + Mizone group ($n = 66$)	PEG group ($n = 66$)	p
Nausea	6 (9.10)	19 (28.80)	0.004
Vomiting	1 (1.50)	7 (10.60)	0.068
Bloating	16 (24.20)	17 (25.80)	0.841
Sleep disturbance	2 (3.00)	4 (6.10)	0.676
Headache	0 (0.00)	1 (1.50)	1.000

Notes: PEG, polyethylene glycol.

Table 6
Biochemical test results before and after bowel preparation in the two groups.

	Preparation protocol	Pre-procedure	Post-procedure	p
Glucose	PEG + Mizone group ($n = 11$)	5.22 ± 1.18	5.09 ± 0.44	0.728
	PEG group ($n = 12$)	5.22 ± 0.70	5.19 ± 0.90	0.915
Potassium	PEG + Mizone group ($n = 11$)	3.80 ± 0.42	3.90 ± 0.41	0.714
	PEG group ($n = 12$)	4.18 ± 0.42	3.98 ± 0.44	0.220
Sodium	PEG + Mizone group ($n = 11$)	140.80 ± 2.70	141.60 ± 2.70	0.497
	PEG group ($n = 12$)	140.60 ± 1.90	142.30 ± 3.90	0.131
Chloride	PEG + Mizone group ($n = 11$)	103.90 ± 3.50	104.00 ± 3.00	0.939
	PEG group ($n = 12$)	103.10 ± 2.20	104.80 ± 3.70	0.152
Bicarbonate	PEG + Mizone group ($n = 11$)	27.20 ± 3.60	26.10 ± 6.80	0.639
	PEG group ($n = 12$)	24.80 ± 2.10	25.20 ± 2.40	0.666
Blood urea nitrogen	PEG + Mizone group ($n = 11$)	5.15 ± 1.50	4.54 ± 1.70	0.389
	PEG group ($n = 12$)	4.77 ± 1.10	5.20 ± 1.60	0.408
Creatinine	PEG + Mizone group ($n = 11$)	63.40 ± 8.60	60.90 ± 12.50	0.592
	PEG group ($n = 12$)	57.80 ± 11.10	60.00 ± 10.50	0.580

Notes: PEG, polyethylene glycol.

Similar to the present finding, Zhang et al. reported that the addition of Mizone does not affect bowel cleanliness [11]. Furthermore, there was no difference in blood glucose, renal function, and serum electrolytes before and after bowel preparation. These present results revealed that the addition of Mizone does not appear to cause a noticeable change in the level of electrolytes, blood glucose, and renal function. These results are similar to those reported by a previous trial that used Gatorade, in conjunction to the PEG solution [34].

The strength of the present study was that a safety assessment was performed, which included blood sampling, before and after taking the laxative. In addition, the present study revealed the optimal Mizone-to-water ratio. For patients who experienced adverse reactions, such as nausea and vomiting, due to poor taste when ingesting PEG, the addition of Mizone would be a good choice. The present study had some limitations. First, the single-center design of the study may have potentially limited the external validity of the findings. Second, the quality of bowel preparation was assessed using a single validated scale. Third, part of the data was obtained using a questionnaire. Thus, a recall bias may have occurred.

5. Conclusion

Combining a vitamin drink (Mizone) with the PEG electrolyte can effectively improve the palatability, and reduce the incidence of nausea and vomiting. This is a safe, well-tolerated preparation for patients, providing comparable effects for bowel cleanliness.

Clinical trial registration statement

The study was registered in the Chinese Clinical Trial Registry (ChiCTR2000034484, https://www.chictr.org.cn/showproj.html?proj=55907).

Informed consent statement

All study participants or their legal guardians provided an informed written consent prior to study enrollment.

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Data availability statement

The data associated to the study has not been deposited to a publicly available repository. The data used and/or analyzed during the study are available from the corresponding author on reasonable request.

CONSORT 2010 statement

The authors have read the CONSORT 2010 statement, and the manuscript was prepared and revised according to the CONSORT 2010 statement.

CRediT authorship contribution statement

Lijie Huang: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Chunjian Li:** Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Data curation. **Yi-Zhou Jiang:** Investigation, Data curation. **Kai Ma:** Investigation, Data curation. **Xiaoyong Wang:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e37590.

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