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Comparison of the Efficacy of Diluted Polyethylene Glycol and Low-Density (0.1% w/v) Barium Sulfate Suspension for CT Enterography

전산화단층촬영 소장조영술을 위한 희석된 폴리에틸렌 글리콜과 저밀도(0.1% w/v) 바륨 현탁액의 유용성 비교

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Purpose To compare small bowel distension and side effects between a diluted polyethylene glycol (PEG) solution and a low-density (0.1% w/v) barium sulfate suspension (LDBSS) for CT enterography (CTE) preparation.

Materials and Methods Total 173 consecutive patients who underwent CTE were enrolled in this study. The LDBSS (1 L) was used in 50 patients, and the diluted iso-osmotic PEG solution (1 L) was used in 123 patients. Two blinded radiologists independently scored jejunal and ileal distensions on a 5-point scale. To compare side effects between the two groups, the patients reported whether they had immediate complications after the administration of the oral contrast media.

Results For ileal and jejunal distension, the diluted PEG solution showed no difference from the LDBSS for either reader (ileum: reader 1, median, 4; 4, interquartile range, 3–4; 3–4, $p = 0.997$; reader 2, median, 4; 4, interquartile range, 3.3–4.0; 3–4, $p = 0.064$; jejunum: reader 1, median, 2; 2, interquartile range, 2–3; 2–3, $p = 0.560$; reader 2, median, 3; 2, interquartile range, 2–3; 2–3, $p = 0.192$). None of the patients complained of immediate complications following administration of either of the oral contrast media.

Conclusion The diluted PEG solution showed comparable bowel distension compared to LDBSS and no immediate side effects; thus, it can be a useful alternative.

Index terms Ileum; Jejunum; Multidetector Computed Tomography; Inflammatory Bowel Disease; Contrast Media; Polyethylene Glycol

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INTRODUCTION

CT enterography (CTE) and MR enterography (MRE) are non-invasive imaging modalities that use a neutral oral contrast agent for luminal distension of the small bowel to enable the evaluation of small bowel pathology in patients with inflammatory bowel disease (IBD) (1). MRE provides high soft tissue contrast and does not require radiation exposure. Despite these advantages, MRE has inherent limitations such as its long examination time, limited availability, and high cost (2). In contrast, CTE has been widely employed and considered a useful imaging tool due to its rapid examination time, easy accessibility, and relatively low cost (3-5).

On CTE, adequate distension of the small bowel lumen facilitates visualization of the anatomy and morphological changes caused by IBD (6). Water itself cannot effect adequate small bowel distension, as it simply passes through the small bowel, causing luminal collapse. Neutral oral contrast media, such as sorbitol, methylcellulose, polyethylene glycol (PEG), mannitol, and low-density (0.1% w/v) barium sulfate suspension have been widely used for sufficient distension of the small bowel. Among these, a low-density (0.1% w/v) barium sulfate suspension leads to adequate small bowel distension with a low rate of side effects (7-10). However, commercial low-density (0.1% w/v) barium sulfate suspension was discontinued in the Korean market, and thus, the necessity for an alternative has emerged.

PEG has been used as a polymeric osmotic laxative for bowel preparation before colonoscopy (11). It is prepared as a powder for mixing with water. As an osmotic laxative, the osmolality of PEG solution reaches 560 mOsm/kg water under the recommended mixture. Therefore, hyperosmotic PEG solution causes osmotic diarrhea because it increases the osmotic pressure between the luminal fluid and bowel wall in the gastrointestinal tract.

At our institution, a diluted PEG solution has been used as an alternative to low-density (0.1% w/v) barium sulfate suspension, given its achievable iso-osmotic (300 mOsm/kg H_2O) status without immediate osmotic diarrhea. To the best of our knowledge, few studies on the application of PEG solution to small bowel distension have been published (12, 13). Furthermore, the empirical use of diluted PEG solution as a small bowel distension agent remains to be validated.

Therefore, the aim of this study was to compare bowel distension and side effects between two neutral oral contrast media, namely, a diluted PEG solution and a low-density (0.1% w/v) barium sulfate suspension, for CTE preparation.

MATERIALS AND METHODS

PATIENT SELECTION

This retrospective study was approved by the Institutional Review Board, and the requirement for informed consent was waived (IRB No. 2022-01-021).

Between January 2018 and October 2021, among patients who had been clinically suspected of IBD, those who satisfied the following inclusion criteria were initially enrolled: 1) those that underwent subsequent CTE, and 2) those that took either a low-density (0.1% w/v) barium sulfate suspension or a diluted PEG solution as a neutral oral contrast media for bowel distension prior to CTE. Accordingly, 173 consecutive patients (127 male and 46 female; mean

age, 34.8 years; range, 18–77 years) were included. A low-density (0.1% w/v) barium sulfate suspension was used for 50 patients, and a diluted PEG solution was used for 123 patients. The case enrollment process is presented in Fig. 1.

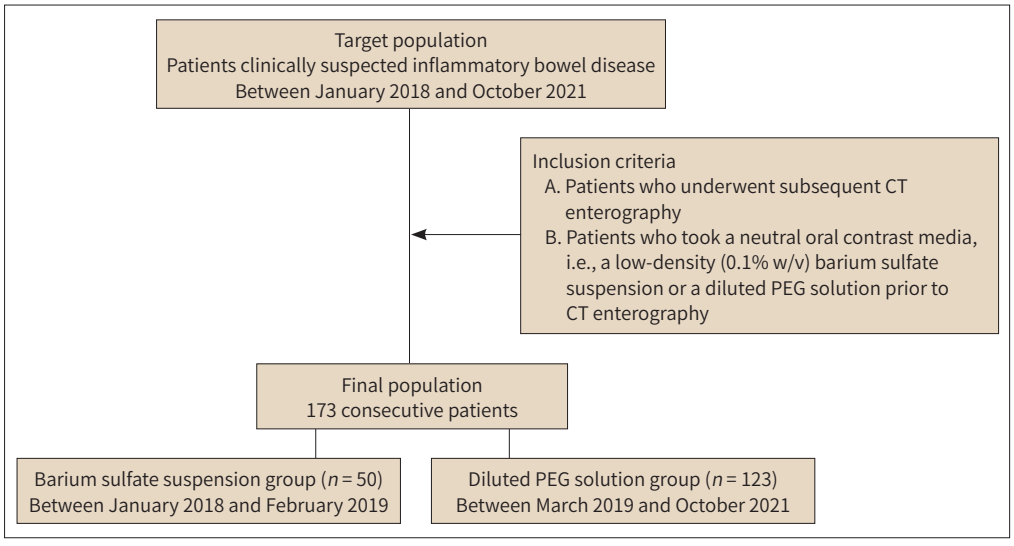
NEUTRAL ORAL CONTRAST MEDIA

The patients were instructed to take 165 mL of a low-density (0.1% w/v) barium sulfate suspension (Easymark; Taejoon Pharm Co. Ltd., Seoul, Korea) every 10 min for 60 min, for a total of 1000 mL, in order to properly distend the small bowel prior to examination. After withdrawal of the low-density (0.1% w/v) barium sulfate suspension from the market, they were instructed to take diluted PEG solution in the same manner. Prior to administration, the diluted PEG solution was prepared by mixing one pack (50 g) of PEG (Coolprep, Taejoon Pharm Co., Ltd.) in 1 L of water. The estimated osmolality was 280 mOsm/kg water, which is very close to the iso-osmolality of 280–300 mOsm/kg water in the human plasma and cerebrospinal fluid. After administration of the oral contrast media, a nurse in the CT preparation room checked the patients' compliance with the oral contrast media by receiving feedback from the patients on whether they experienced immediate nausea, vomiting, diarrhea, or abdominal cramping pain.

CT PROTOCOL

All of the CT examinations were performed using a 64-multidetector CT scanner (Discovery CT 750HD; GE Healthcare, Milwaukee, WI, USA) after intravenous injection of 1.5 mL/kg of iohexol (Iobrix 300®; Taejoon Pharm Co. Ltd.) at a rate of 3 mL/s via the antecubital vein. CT images were acquired in the enteric phase using a fixed time delay method, 45 s after intravenous injection of the contrast media. Image reconstructions were acquired using conventional filtered back projection with a reference noise index of 16, and coronal reformatted images were obtained at thicknesses of 3 mm. The detailed scan parameters were as follows: fixed tube potential, 120 kV; tube current range, 90–210 mA, with activated automatic expo-

Fig. 1. Flowchart of the case enrollment process of the patients.



PEG = polyethylene glycol

sure control; detector configuration, 64 × 0.625 mm; gantry rotation time, 0.5 seconds; pitch, 0.984; helical acquisition mode; and section thickness, 5 mm.

QUALITATIVE ANALYSIS

For the qualitative analysis of small bowel distension, two radiologists, both of whom were blinded to the patients' clinical information and had 4 years of experience in reading CTE independently, scored the grades for distension of the jejunum and ileum on a 5-point scale (1, collapse; 2, a portion of the adequately distended segment is less than 50%; 3, a portion is in the 50%–80% range; 4, a portion is distended > 80% but ≤ 100%; 5, full distension of the total segment). Adequate distension was defined as a small bowel diameter larger than 1.5 cm. Coronal images were provided due to their usefulness for assessing the small bowel's anatomical location (14). The global locations where the oral contrast media were mainly distributed were recorded as gastric, colonic, or evenly distributed.

QUANTITATIVE ANALYSIS

For quantitative analysis, another radiologist, who had three years of experience in reading CTE and was also blinded to the patients' information, measured the diameter of the lumen in the jejunum and ileum. Measurements were made at the proximal, mid, and distal portions of both the ileum and jejunum and then averaged.

STATISTICAL ANALYSIS

Statistical analyses were performed using Windows software (MedCalc version 20.113; Mariakierke, Belgium). Differences were considered statistically significant when the *p*-value was less than 0.05. Demographic data were compared between the two groups using the *t*-test or chi-square test. In addition, the Mann–Whitney U test was used to compare the grades of small bowel distension between the two groups, and the diameters of the small bowel were compared using *t*-test. To determine the inter-observer agreement for small bowel distension, the weighted kappa value was calculated and interpreted as poor (≤ 0.20), fair (0.21–0.40), moderate (0.41–0.60), good (0.61–0.80), or excellent (0.81–1.00) (15).

RESULTS

DEMOGRAPHICS OF THE STUDY POPULATION

Of 173 consecutive patients, the study population consisted of patients with Crohn's disease (*n* = 122, 71%, *p* = 0.794), non-specific enteritis (*n* = 33, 19%, *p* = 0.131), tuberculous enterocolitis (*n* = 4, 2%), ulcerative colitis (*n* = 1, 1%), Behcet's disease (*n* = 5, 3%), tumor (*n* = 7, 4%), or vasculitis (*n* = 1, 1%). The demographics of the study population are presented in Table 1.

QUALITATIVE ANALYSIS

For ileal distension, the diluted PEG solution showed no significant difference from the barium sulfate suspension for either reader (reader 1, median, 4; 4, interquartile range, 3–4; 3–4, *p* = 0.997; reader 2, median, 4; 4, interquartile range, 3.3–4.0; 3–4, *p* = 0.064) (Fig. 2). For both readers, the numbers of patients corresponding to each grade for ileal distension with

Table 1. Demographics of the Study Population

Parameter	Barium Sulfate Suspension (*n* = 50)	Diluted PEG Solution (*n* = 123)	Total (*n* = 173)	*p*-Value
Age, median [range]	28 [18–74]	32 [19–77]	30 [18–77]	0.358
Sex, male/female	37/13	90/33	127/46	0.914
Diagnosis				
Crohn's disease	36 (72)	86 (70)	122 (71)	0.794
Non-specific enteritis	6 (12)	27 (22)	33 (19)	0.131
Tbc enterocolitis	3 (6)	1 (1)	4 (2)	
Ulcerative colitis	0 (0)	1 (1)	1 (1)	
Behcet's disease	2 (4)	3 (2)	5 (3)	
Tumor	3 (6)	4 (3)	7 (4)	
Vasculitis	0 (0)	1 (1)	1 (1)	

Data are presented as the number (%) of patients.
**p*-values were calculated using the *t*-test or chi-square test.
PEG = polyethylene glycol

the diluted PEG solution and barium sulfate suspension were as follows: reader 1, grade 1, 2/0; grade 2, 25/8; grade 3, 16/10; grade 4, 77/32; grade 5, 3/0; reader 2, grade 1, 0/0; grade 2, 10/9; grade 3, 21/10; grade 4, 88/30, grade 5, 4/1.

For jejunal distension, the diluted PEG solution showed comparable distension to that of the barium sulfate suspension for both readers (reader 1, median, 2; 2, interquartile range, 2–3; 2–3, $p = 0.560$; reader 2, median, 3; 2, interquartile range, 2–3; 2–3, $p = 0.192$) (Fig. 3). For both readers, the numbers of patients corresponding to each grade for jejunal distension with the diluted PEG solution and barium sulfate suspension were as follows: reader 1, grade 1, 1/0; grade 2, 63/29; grade 3, 38/13; grade 4, 20/8; grade 5, 1/0; reader 2, grade 1, 7/1; grade 2, 21/25; grade 3, 41/19; grade 4, 53/5, grade 5, 1/0. A comparison of the results is presented in Table 2 and Fig. 4.

The global distribution of where the oral contrast media were mostly located is presented in Table 3. There was no significant difference between the two different oral contrast media for either reader (reader 1: gastric predominance, $p = 0.514$; colonic predominance, $p = 1.000$; even distribution, $p = 0.585$; reader 2: gastric predominance, $p = 0.184$; colonic predominance, $p = 0.410$; even distribution, $p = 0.103$).

In terms of inter-observer agreement for ileal and jejunal distension, the diluted PEG solution showed good and excellent agreement (kappa = 0.614 and 0.827, respectively), and the barium sulfate suspension showed moderate and good agreement (kappa = 0.491 and 0.752, respectively). The kappa values for the diluted PEG solution and barium sulfate suspension for ileal and jejunal distension between the two readers are summarized in Table 4.

QUANTITATIVE ANALYSIS

For ileal distension, the diluted PEG solution showed no significant difference from the barium sulfate suspension (mean [cm] ± standard deviation [cm], 2.0 ± 0.4, 1.9 ± 0.3, respectively, $p = 0.126$); the same was true for jejunal distension (mean [cm] ± standard deviation [cm], 1.9 ± 0.3, 1.9 ± 0.2, respectively, $p = 0.845$).

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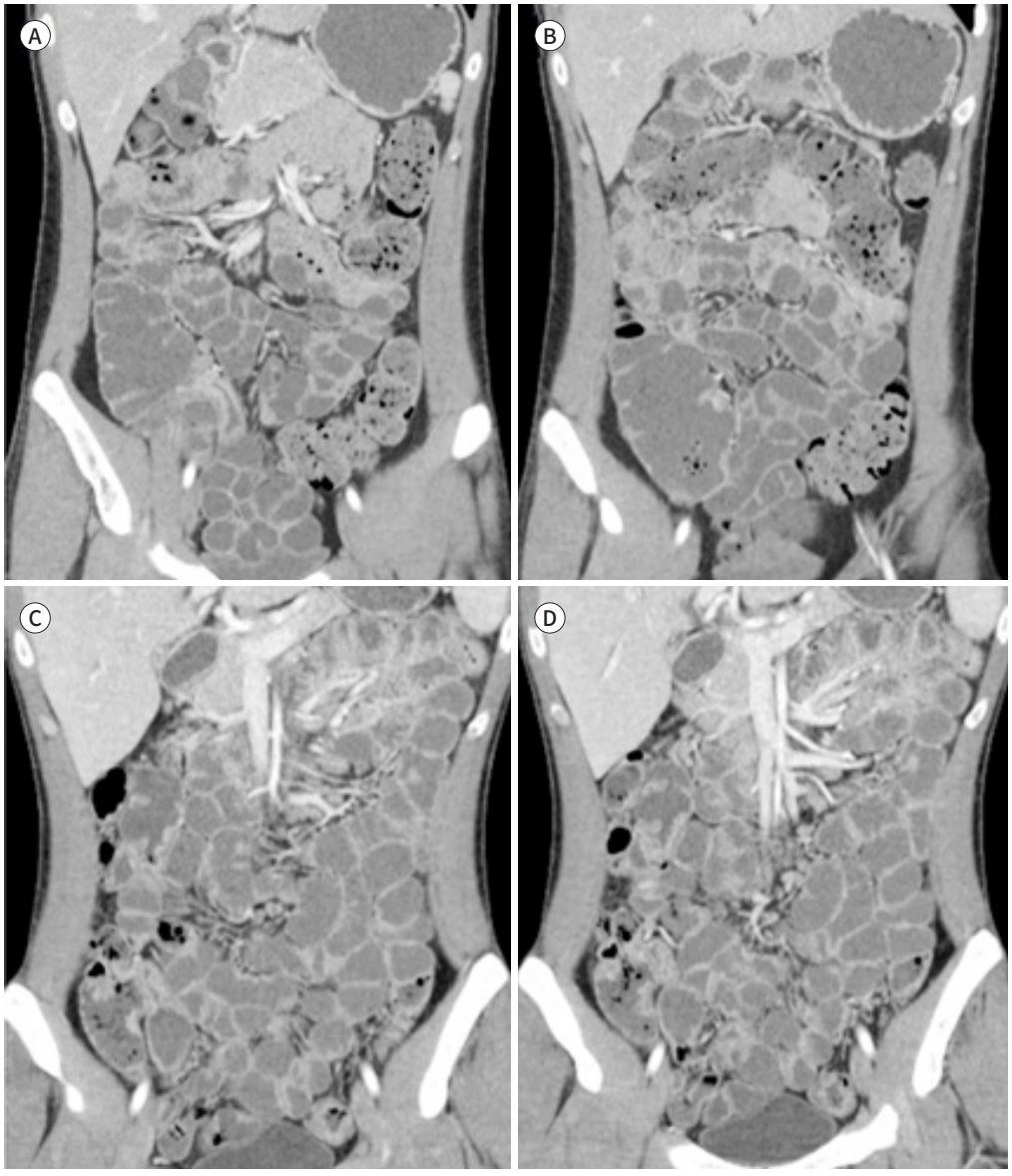
Fig. 2. Coronal reformatted images for comparison of ileal distension between diluted polyethylene glycol solution (A, B) and low-density (0.1% w/v) barium sulfate suspension (C, D). For ileal distension, both readers allocated scores of 4 or 5 to both of the oral contrast media. A score of 4 indicates that the portion of the adequately distended segment is greater than 80% and less than 100%, while a score of 5 indicates full distention of the total segment.



In terms of the diluted PEG solution, ileal distension was better than jejunal distension (mean [cm] ± standard deviation [cm], 2.0 ± 0.4, 1.9 ± 0.3, respectively, $p < 0.001$). Regarding the barium sulfate suspension, ileal distension was comparable to jejunal distension (mean [cm] ± standard deviation [cm], 1.9 ± 0.3, 1.9 ± 0.2, respectively, $p = 0.689$).

The measured diameters (cm) of the jejunum and ileum were as follows: for the proximal, mid, and distal jejunum, 2.0 ± 0.4, 1.9 ± 0.3, and 1.9 ± 0.4, respectively; for the proximal, mid, and distal ileum, 1.9 ± 0.4, 2.0 ± 0.4, and 2.0 ± 0.4, respectively.

Fig. 3. Coronal reformatted images for comparison of jejunal distension between diluted PEG solution (A, B) and low-density (0.1% w/v) barium sulfate suspension (C, D). For jejunal distension, both readers allocated scores of 4 to both of the oral contrast media. A score of 4 indicates that the portion of the adequately distended segment was greater than 80% and less than 100%.

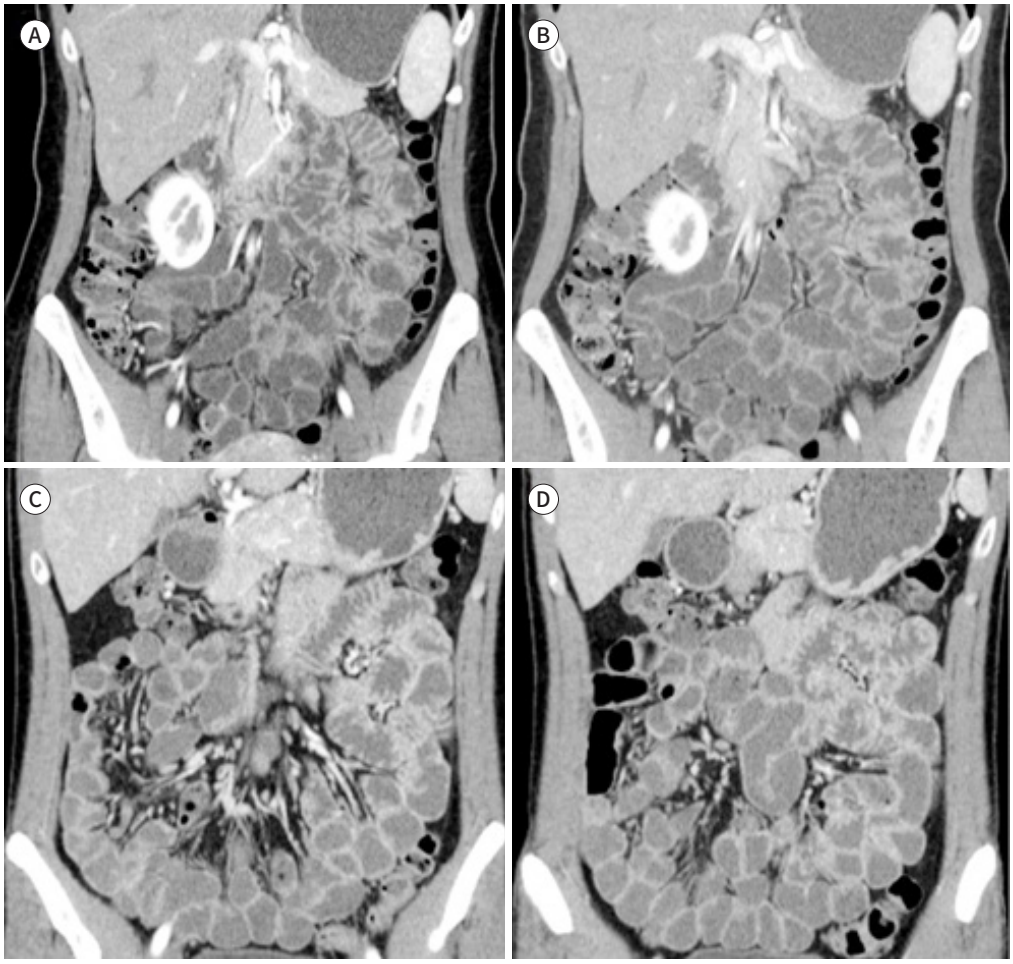


Table 2. Results of Bowel Distension between Two Oral Contrast Media

	Barium Sulfate Suspension	Diluted PEG Solution	*p*-Value*
Reader 1			
Jejunum	2 (2.0–3.0)	2 (2.0–3.0)	0.560
Ileum	4 (3.0–4.0)	4 (3.0–4.0)	0.997
Reader 2			
Jejunum	2.0 (2.0–3.0)	3.0 (2.0–3.0)	0.192
Ileum	4.0 (3.0–4.0)	4.0 (3.3–4.0)	0.064

Data are presented as both the median and interquartile range (in parenthesis) on a 5-point scale (1, collapse; 2, a portion of the adequately distended segment is less than 50%; 3, a portion is in the 50%–80% range; 4, a portion is distended > 80% but ≤ 100%; 5, optimally distended).
**p*-values were calculated using the Mann-Whitney U test.
PEG = polyethylene glycol

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PATIENT COMPLIANCE WITH ORAL CONTRAST MEDIA

No CTE failure occurred. Regarding the patients' compliance with the two different oral contrast media, none of the patients complained of immediate nausea, vomiting, diarrhea, or abdominal cramping pain for either oral contrast media.

Fig. 4. Histogram of the grades for small bowel distension with a diluted PEG solution and low-density (0.1% w/v) barium sulfate suspension.
PEG = polyethylene glycol

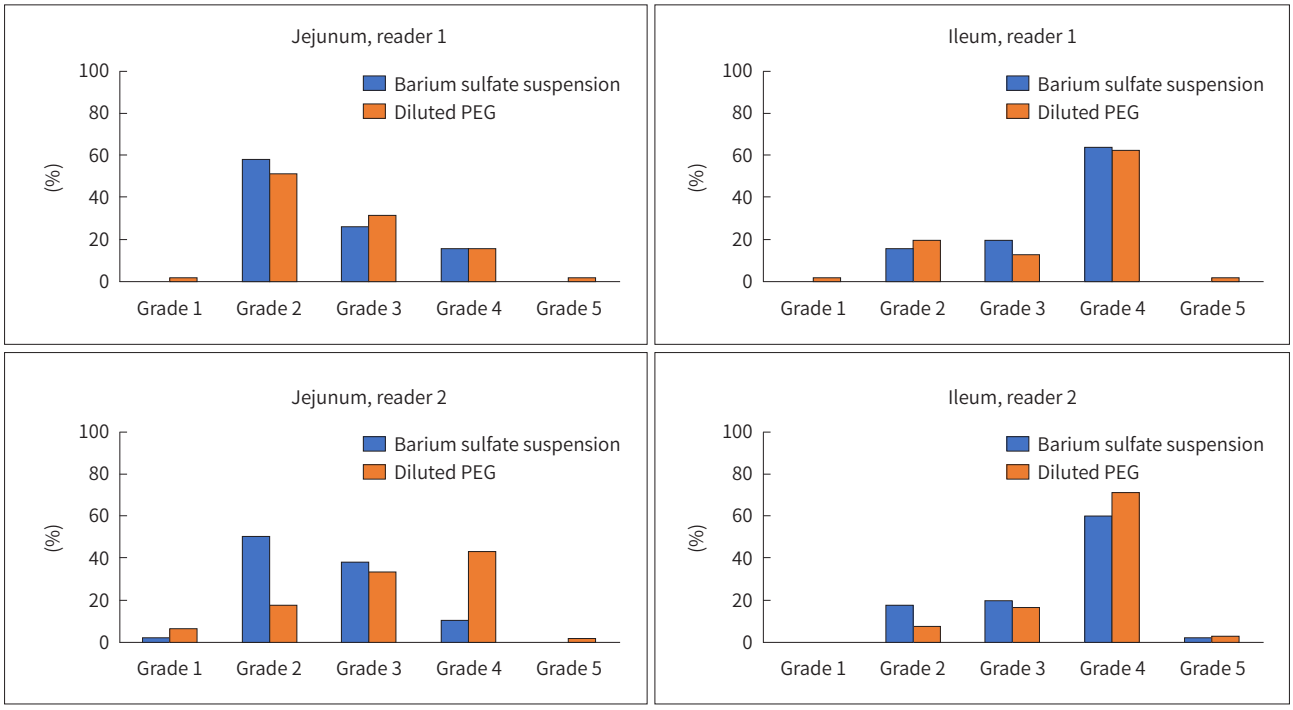

Table 3. Global Distributions of Oral Contrast Media in the Gastrointestinal Tract

	Reader 1			Reader 2		
	Diluted PEG Solution	Barium Sulfate Suspension	*p*-Value	Diluted PEG Solution	Barium Sulfate Suspension	*p*-Value
Gastric predominance	11 (9)	3 (6)	0.514	11 (9)	8 (16)	0.184
Colonic predominance	5 (4)	2 (4)	1.000	10 (8)	6 (12)	0.410
Even distribution	107 (87)	45 (90)	0.585	102 (83)	36 (72)	0.103

Data are presented as the number (%) of patients.
PEG = polyethylene glycol

Table 4. Inter-Observer Agreement for Bowel Distension

	Diluted PEG Solution	Barium Sulfate Suspension
Ileum	0.614 (0.492–0.735)	0.491 (0.224–0.759)
Jejunum	0.827 (0.763–0.891)	0.752 (0.616–0.889)

Data are presented as both the weighted kappa value and 95% confidence interval (in parenthesis). The kappa value was interpreted as follows: poor (≤ 0.20), fair (0.21–0.40), moderate (0.41–0.60), good (0.61–0.80) or excellent (0.81–1.00).
PEG = polyethylene glycol

DISCUSSION

Our results revealed that the bowel distension efficacies of the diluted PEG solution and barium sulfate suspension were comparable for both the ileum and jejunum in qualitative and quantitative analyses. Notably, our results correspond well with the results of Gottumukkala et al. (7), who reported that the mean small bowel diameters of patients who took a PEG solution were non-inferior to those of patients who took a low-concentration (0.1%) barium sulfate suspension. In addition, the mean ratings of overall bowel distension did not significantly differ among the groups of pediatric patients with Crohn's disease prior to MRE in their study. Correspondingly, the ratings of well-being following contrast administration did not differ significantly between the groups. These similar results may be attributed to the fact that the estimated osmolality of the PEG solution was 400 mOsm/kg water, which is relatively close to the osmolality observed in our study.

The PEG solution was used for small bowel distension in two previous studies (12, 13) conducted in Korea. However, neither the concentration of the PEG solution nor the administration regimen was specified in either study. As a laxative having a 560 mOsm/kg water osmolality, PEG has been used in colonoscopy preparation. Thus, non-diluted PEG can cause osmotic diarrhea when taking it for an hour before or during CTE. In such cases, the examination may fail, or the small bowel may not distend sufficiently. Furthermore, as patients must take a total amount of 1.5 L, compliance tends to be decreased, and there is a potential for side effects such as nausea, diarrhea, abdominal distension, and pain (16).

In terms of the side effects discussed above, Singla et al. (17) compared the side effects of four oral contrast agents with the same 1.5 L, specifically 3% mannitol solution, PEG solution, iohexol solution, and plain water prior to CTE. Among the side effects, nausea was the second most common in the PEG solution group after the iohexol solution group, and diarrhea was reported in eight patients in the mannitol group; however, this was not observed in the remaining groups. The reason side effects were common in the mannitol and PEG solution groups may be associated with the high osmolality of the oral contrast media, as the estimated osmolality of the mannitol and PEG solution were 670 and 560 mOsm/kg water, respectively.

In a different study to that above, Young et al. (18) compared the side effects of oral contrast agents with water, methylcellulose, PEG solution, and low-concentration (0.1% w/v) barium sulfate suspension for MRE preparation. The frequency and severity of nausea and diarrhea 24 h after ingestion of each agent were rated (18). Of note, the mean ratings of nausea and diarrhea for the PEG solution were higher than those of the other oral contrast agents. The discrepancy between Young's results (18) and ours could be explained by several reasons, including their undiluted use of PEG, 24-hour-duration of reporting the side effects, and small study population of 10 patients. In contrast, we only observed immediate side effects after the ingestion of oral contrast media prior to CTE, which is a limitation of the present study. However, the current study population was larger than that of the previous study, which is a strength of our study. Notably, sorbitol is an alternative contrast agent for CTE preparation (7, 8, 19, 20); however, it is not easy to prepare a proper solution by mixing sorbitol powder with water prior to CTE. In addition to sorbitol, other neutral oral contrast agents used for small bowel distension include low-density (0.1% w/v) barium sulfate suspension, mannitol, and

methylcellulose (7, 8, 17-20).

In the present study, the diluted PEG solution showed good and excellent interobserver agreement for ileal and jejunal distension, respectively. Regarding the global distribution of oral contrast media in the gastrointestinal tract, the diluted PEG solution showed a predominantly even distribution, which was also the case with the low-density barium sulfate suspension. In addition to bowel distension, rare side effects, and patients' tolerability, sustained inter-observer agreement and globally even distributions of orally administered media are also important requirements for alternatives to the low-density (0.1% w/v) barium sulfate suspension. Based on this fact as well as previous observations in the literature and our present data, we suggest that the diluted PEG solution can be effectively employed for small bowel distension for CTE preparation.

This study has some limitations. First, the study population predominantly consisted of patients with IBD, particularly Crohn's disease. However, this is reflective of our daily practice in that patients with suspected IBD usually undergo CTE. Second, small bowel distension could be over- or underestimated in patients with IBD complications, such as ileus or stenosis. For this reason, our third radiologist made an effort to measure the small bowel diameter at three different sites in the jejunum and ileum and avoided the stenotic portion as much as possible. Third, there is a slightly limited interpretation of the interobserver agreement for small bowel distension in this study due to the discrepancy in the study population number between the two groups.

In conclusion, the diluted PEG solution showed similar efficacy for bowel distension to that of the low-density (0.1% w/v) barium sulfate suspension for CTE preparation.

Author Contributions

Conceptualization, K.S.H.; data curation, K.Y.J., K.S.H.; formal analysis, K.S.H.; funding acquisition, K.S.H.; investigation, all authors; methodology, K.S.H.; project administration, K.S.H.; resources, K.S.H.; software, K.S.H.; supervision, K.S.H.; validation, all authors; visualization, K.Y.J., K.S.H.; writing—original draft, all authors; and writing—review & editing, all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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전산화단층촬영 소장조영술을 위한 희석된 폴리에틸렌 글리콜과 저밀도(0.1% w/v) 바륨 현탁액의 유용성 비교

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목적 전산화단층촬영 소장조영술 준비를 위해서 사용된 중성 경구 조영제인 희석된 폴리에틸렌 글리콜 용액과 저밀도(0.1% w/v) 바륨 현탁액 사이의 소장 팽창과 부작용을 비교하였다.

대상과 방법 전산화단층촬영 소장조영술을 시행 받은 총 173명의 환자가 연구에 포함되었다. 50명의 환자는 바륨 현탁액을, 123명의 환자는 희석된 등삼투압의 폴리에틸렌 글리콜 용액을 사용하였다. 동일한 양인 1L를 투여하였다. 두 명의 독립된 검토자가 공장과 회장에서 5점 척도로 소장 팽창을 평가하였다. 두 그룹 간의 부작용 비교를 위해서 경구 조영제 투입 후 환자들이 구역, 구토, 설사 및 복통을 호소하는지 여부에 대하여 조사하였다.

결과 회장과 공장에서, 희석된 폴리에틸렌 글리콜 용액은 두 검토자 모두에서 바륨 현탁액과 차이가 없었다(회장: 검토자 1, 중앙값, 4; 4, 사분위수 범위, 3–4; 3–4, $p = 0.997$; 검토자 2, 중앙값, 4; 4, 사분위수 범위, 3.3–4.0; 3–4, $p = 0.064$, 공장: 검토자 1, 중앙값, 2; 2, 사분위수 범위, 2–3; 2–3, $p = 0.560$; 검토자 2, 중앙값, 3; 2, 사분위수 범위, 2–3; 2–3, $p = 0.192$). 모든 환자에서 두 가지 경구 조영제 투여 후 즉각적인 부작용을 호소하지 않았다.

결론 희석된 폴리에틸렌 글리콜 용액은 바륨 현탁액과 비교하여 소장 팽창에 차이가 없고, 검사 직후 부작용이 없으므로, 유용한 대체제가 될 수 있다.

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