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나이에 따른 대장정결과 관련된 위병증: 경구황산염 정제와 1리터 폴리에틸렌 글리콜

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Acute Gastropathy Associated with Bowel Preparation According to Age: Oral Sulfate Tablets versus 1-L Polyethylene Glycol with Ascorbic Acid

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Background/Aims: The use of 1-L polyethylene glycol with ascorbate (PEG/Asc) and oral sulfate tablets (OST) as low-volume bowel preparation agents has gradually increased. However, these agents may induce acute gastropathy during bowel preparation, particularly in elderly populations. This study aimed to compare the incidence of acute gastropathy of 1-L PEG/Asc and OST according to age, as well as efficacy and safety.
Methods: This retrospective study included patients who underwent esophagogastroduodenoscopy (EGD) and colonoscopy for screening on the same day and underwent bowel preparation using OST or 1-L PEG/Asc. We collected EGD findings related to acute gastropathy, bowel-cleansing score using the Boston Bowel Preparation Scale (BBPS), polyp or adenoma detection rate (ADR), and laboratory parameters.
Results: Of 4,711 patients, 1,758, 2,241, and 712 were in the younger (18–49 years), middle-aged (50–64 years), and older (≥65 years) groups, respectively. In all age groups, the OST group had higher rates of acute gastropathy than the 1-L PEG/Asc group. The younger-, middle-, and older-aged groups had OST and 1-L PEG/Asc usage rates of 42.9% and 11.6%, 41.2% and 16.0%, and 41.5% and 16.4%, respectively. Notably, in the younger group, the total BBPS and ADR scores were significantly higher in the OST group than in the 1-L PEG/Asc group; however, these did not differ in the other age groups.
Conclusions: Acute gastropathy was more strongly associated with OST than with 1-L PEG/Asc in all age groups. Therefore, physicians should consider acute gastropathy associated with low-volume agents in all age groups when performing bowel preparation. **(Korean J Gastroenterol 2024;84:177-187)**

Key Words: Cathartics; Oral sulfate tablet; Polyethylene glycols; Gastropathy; Colonoscopy

INTRODUCTION

Colonoscopy is the gold standard for the early detection of colorectal cancer (CRC) and the removal of precancerous polyps.[1,2] Clear visualization of the entire colonic mucosa is essential for an effective colonoscopy, and this requires a large volume of fluid to pass into the colonic lumen for bowel preparation.[3] Traditionally, a 4-L isotonic solution containing polyethylene glycol (PEG) with an electrolyte has been used to induce osmotic activity, causing profuse diarrhea. However,

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to improve poor compliance caused by taking large volumes, ascorbate, a hypertonic osmotic substance, has been combined with 2-L PEG to reduce the volume of fluid intake. Recently, a 1-L PEG plus ascorbate (1-L PEG/Asc) preparation was developed to further reduce the solution volume by increasing the ascorbate content.[4] Additionally, a new formulation of oral sulfate solution (OSS), consisting of sodium sulfate, potassium sulfate, and magnesium sulfate, has been developed for low-volume bowel preparation; however, the high sulfate content of OSS results in a rotten egg smell and bitter taste.[5-7] To improve compliance by eliminating the unpleasant experience of using OSS, an oral sodium sulfate tablet (OST) has recently been developed as a bowel preparation agent in tablet format, with a tasteless and odorless nature.[8] In fact, in randomized clinical trials, OST had better bowel preparation efficacy (particularly in the right colon), higher compliance, and better safety than 1-L PEG/Asc and 2-L PEG/Asc , as well as no inferior adenoma detection rate (ADR).[8-12] Therefore, the use of 1-L PEG/Asc and OST as low-volume bowel preparation agents has gradually increased.

These low-volume bowel preparation agents have raised concerns regarding the risk of acute gastric mucosal injury due to incomplete dissolution of the tablet formula in water or hyperosmolarity originating from the concentrated solution.[13-16] In fact, a recent study has reported that OST may induce erosive gastritis.[17] Even if these lesions have not yet been determined to be clinically significant, a positive finding upon esophagogastroduodenoscopy (EGD) can influence endoscopic interpretation. Nevertheless, insufficient data on acute gastropathy due to the use of these bowel preparation agents limits the choice of low-volume agents for bowel preparation.

The elderly population is less likely to tolerate high-volume agents; therefore, the availability of low-volume agents is crucial for planning colonoscopies in elderly patients.[18,19] However, because old age is a known risk factor for inappropriate bowel preparation and poor safety, elderly individuals have often been excluded from clinical trials of low-volume agents subjects have often been excluded from clinical trials with low-volume agents because old age has been known as a risk factor for inappropriate bowel preparation and vulnerable safety and few randomized controlled trials reported the efficacy and safety of low-volume agents in elderly subjects.[18,20] Moreover, despite the increasing burden of elderly patients undergoing colonoscopy, no previous study has reported safety data for acute gastric mucosal lesions associated with low-volume agents such as 1-L PEG/Asc and OST in elderly subjects.

Therefore, we compared the incidence of acute gastropathy and the efficacy, and safety of 1-L PEG/Asc and OST according to age in healthy subjects who underwent both EGD and colonoscopy.

SUBJECTS AND METHODS

1. Study design and population

This retrospective study included patients visiting the Health Promotion Center of a single academic hospital in South Korea between January 1, 2021, and December 31, 2022. Eligible participants included outpatients aged ≥18 years who underwent a scheduled EGD and colonoscopy on the same day for screening and were administered only OST (Orafang®; Pharmbio Korea Co. Ltd., Seoul, Korea) or 1-L PEG/Asc (CleanViewAL®; Taejoon Pharm Co., Ltd., Seoul, Korea) for bowel preparation before colonoscopy. Bowel preparation agents were selected by the subject's preference as much as possible, and doctor's recommendation was not intervened in the selection process. The study population was divided into three age groups as follows: those aged 18–49, 50–64, and ≥65 years were defined as the young, middle-aged, and old-aged groups, respectively. We collected patient demographic data, comorbidities, current medication use, EGD and colonoscopy findings, bowel preparation results, and several laboratory parameters from the day of the colonoscopy.

This study was approved by the Institutional Review Board of our study institution (KHNMC IRB 2023-10-037) and conducted according to the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. Informed consent was waived by KHNMC IRB because of the retrospective study design.

2. Bowel preparation protocol

All participants were instructed to follow a low-residue diet for 3 days before the scheduled colonoscopy and a clear liquid diet for dinner the night before the colonoscopy. Both groups received preparation agents as a split-dosing regimen at home. The first dose was administered between 6:00 and 8:00 PM the day before the colonoscopy, while the second dose was administered between 6:00 and 8:00 AM on the day of the

colonoscopy, at least 3 hours before the scheduled procedure. All patients underwent EGD and colonoscopy between 9:00 AM and noon. Patients in the OST group took the first sequence of 14 tablets with water and an additional 1 L of water over an hour, as well as a second sequence of the remaining 14 tablets, similar to the first. In contrast, patients in the 1-L PEG/Asc group were instructed to drink 500 mL of the study solution - a mixture of the study drug in powdered form and free water - followed by at least 500 mL of free water per dose.

3. Assessment of outcomes

The primary outcome of this study was the presence of acute gastropathy associated with bowel preparation agents in the EGD findings. In this study, acute gastric lesions caused by bowel preparation agents were divided into three categories: hyperemia, erosive lesions, and acute gastric mucosal lesion (AGML)-like blood clots or hematin (Fig. 1). The location of the occurrence of acute gastric lesions was distinguished from other locations by the greater curvature (GC) of the body of the stomach, which frequently occurs due to its dependent position.[21] The severity of gastric mucosal injury was evaluated using the LANZA score based on five grades as follows: normal stomach or proximal duodenum=0, mucosal hemorrhage only=1, one or two erosions=2, numerous (3–10) erosions=3, and a large number of erosions (>10) or ulcers=4.[22] In addition, retention of fluid ≥200 mL was recorded upon each EGD examination. The presence of gastropathy associated with bowel preparation agents was reviewed by four non-investigating gastroenterologists who were blinded to the administered preparation agents.

In this study, we used the Boston Bowel Preparation Scale (BBPS) for the bowel preparation score. The BBPS is a 4-point (0–3) scale used to assess three segments of the colon, namely, the right (cecum and ascending colon), transverse, and left (descending, sigmoid colon, and rectum) segments, giving a total score of 0 to 9.[23] Successful overall bowel preparation was defined as a BBPS score ≥2 for all segments, while high-quality bowel preparation was defined as a BBPS score of 9. Bowel cleansing scores were evaluated by highly experienced board-certified gastroenterologists who performed the endoscopic procedures. Other secondary outcomes included the polyp detection rate (PDR), ADR, and CRC rate. The PDR and ADR were calculated as the percentage of patients in the analyzed population with at least one polyp or adenoma, respectively. Furthermore, the study population underwent laboratory testing to determine serum levels of blood urea nitrogen (BUN), sodium, potassium, chloride, calcium, and phosphate on the day of the colonoscopy (post-bowel preparation).

4. Statistical analysis

Continuous variables are presented as the mean±standard deviation for clinical data and were compared using two-sample t-tests. In contrast, categorical variables are presented as numbers and percentages. These were analyzed using the chi-squared test or Fisher's exact test for comparison between two groups and analysis of variance or the Kruskal–Wallis test for comparison between three groups. All statistical analyses were performed using SPSS software (version 20.0; IBM Corp., Armonk, NY, USA), and all statistical tests were two-sided with statistical significance set at $p<0.05$. The distribution of each laboratory parameter after the study medication was administered was determined as an overlay graph using the kernel density plot in Stata 16.1 software (StataCorp LP, College Station, TX, USA).

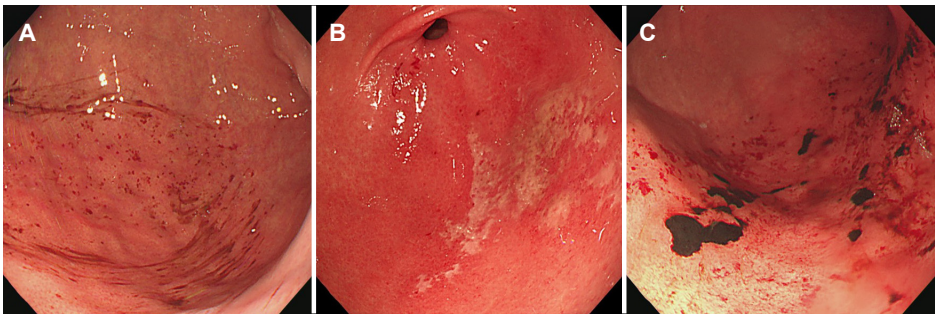

Fig. 1. Esophagogastroduodenoscopic findings of acute gastropathy: (A) hyperemia, (B) erosive lesions, and (C) acute gastric mucosal lesion-like blood clots or hematins.

RESULTS

1. Patient characteristics

Table 1 shows the baseline characteristics of the study population according to the age group. Of the 4,711 participants, the mean ages of the young (n=1,758), middle-aged (n=2,241), and old-aged (n=712) groups were 40.8, 56.7, and 69.2 years, respectively. There were no significant differences in sex or BMI distribution between the three groups. However, among the comorbid diseases, ischemic heart disease (p=0.045), malignancy (p<0.001), and cerebrovascular disease (p<0.001) were more prevalent in the older group than in the other age groups. Moreover, the rate of current medication use – including non-steroidal anti-inflammatory drugs (NSAIDs), antiplatelet agents, and anticoagulants – increased with age (p<0.001). Notably, the middle- and old-aged groups preferred OST for bowel preparation, whereas the young group preferred 1-L PEG/Asc (p<0.001).

Table 1. Baseline Characteristics of the Study Population According to Age

Baseline characteristics	Young age (18–49 years) (n=1,758)	Middle-aged (50–64 years) (n=2,241)	Old-aged (≥65 years) (n=712)	p-value
Age (years)	40.8±5.8	56.6±4.2	69.2±3.7	<0.001
Sex				
Male	1,070 (60.9)	1,318 (58.8)	410 (59.4)	0.240
Female	688 (39.1)	923 (41.2)	302 (42.4)	
BMI				
≥25 kg/m^2	619 (35.2)	788 (35.2)	240 (33.7)	0.748
<25 kg/m^2	1,139 (64.8)	1,453 (64.8)	472 (66.3)	
Comorbid disease				
Hypertension	92 (5.2)	111 (5.0)	31 (4.4)	0.660
Diabetes mellitus	97 (5.5)	107 (4.8)	23 (3.2)	0.055
Ischemic heart disease	90 (5.1)	133 (5.9)	55 (7.7)	0.045
Malignancy	39 (2.2)	144 (6.4)	86 (12.1)	<0.001
Cerebrovascular disease	8 (0.5)	24 (1.1)	19 (2.7)	<0.001
Current medication use				
Antiplatelet agent	24 (1.4)	200 (8.9)	174 (24.4)	<0.001
Anticoagulant	0 (0.0)	8 (0.4)	14 (2.0)	<0.001
Non-steroidal anti-inflammatory drug	22 (1.3)	48 (2.1)	30 (4.2)	<0.001
Bowel-preparation agent				
Oral sulfate tablet	822 (46.8)	1,422 (63.5)	407 (57.2)	<0.001
1-L PEG/Asc	936 (53.2)	819 (36.5)	305 (42.8)	

Values are presented as mean±standard deviation or number (%).
BMI, body mass index; PEG/Asc, polyethylene glycol with ascorbate.

Table 2. Acute Gastropathy Upon Esophagogastroduodenoscopy after Taking a Bowel Cleansing Agent According to Age Group

Acute gastropathy	Young age (18–49 years) (n=1,758)			Middle-aged (50–64 years) (n=2,241)			Old-aged (≥65 years) (n=712)		
	OST (n=822)	1-L PEG/Asc (n=936)	p-value	OST (n=1,422)	1-L PEG/Asc (n=819)	p-value	OST (n=407)	1-L PEG/Asc (n=305)	p-value
Acute gastropathy[a]									
Any lesion	359 (43.7)	113 (12.1)	<0.001	594 (41.8)	137 (16.7)	<0.001	169 (41.5)	53 (17.4)	<0.001
AGML-like blood clots or hematins	134 (16.3)	31 (3.3)	<0.001	251 (17.7)	51 (6.2)	<0.001	73 (17.9)	16 (5.2)	<0.001
Erosions or hyperemia at GC/body	337 (41.0)	82 (8.8)	<0.001	538 (37.8)	104 (12.7)	<0.001	157 (38.6)	46 (15.1)	<0.001
Erosions at the rest sites[b]	316 (38.4)	84 (9.0)	<0.001	506 (35.6)	115 (14.0)	<0.001	150 (36.9)	46 (15.1)	<0.001
Hyperemia at the rest sites[b]	97 (11.8)	24 (2.6)	<0.001	139 (9.8)	34 (4.2)	<0.001	36 (8.8)	8 (2.6)	0.001
Fluid retention ≥200 mL	67 (8.2)	118 (12.6)	0.002	84 (5.9)	60 (7.3)	0.187	12 (2.9)	18 (5.9)	0.052

Values are presented as number (%).
AGML, acute gastric mucosal lesion; GC, greater curvature; NA, not available; OST, oral sulfate tablet; PEG/Asc, polyethylene glycol with ascorbate.
[a]All overlapping cases were included. [b]All sites except the GC of the body of the stomach.

2. Acute gastropathy associated with preparation

In all age groups, acute gastropathy lesions were observed at higher rates in the OST group than in the 1L-PEG/Asc group (Table 2). Moreover, in the young age group, AGML-like blood clots or hematins occurred approximately five times more frequently in the OST group than in the 1-L PEG/Asc group (16.3% vs. 3.3%), while this was approximately three-fold in the middle-aged (17.7% vs. 6.2%) and old-aged (17.9% vs. 5.2%) groups. Within the OST group, there was no significant difference in the occurrence of acute gastropathy according to age. However, in the 1-L PEG/Asc group, the old-aged group showed a more frequent occurrence of acute gastropathy. Furthermore, cases with fluid retention in the stomach of >200 mL occurred more commonly in the 1-L PEG/Asc group than in the OST group, and this occurred more frequently in younger patients.

Fig. 2 shows the distribution of gastric mucosal injury severity based on the LANZA score. Notably, in the young age group, 56.3% and 87.9% of the patients in the OST and 1-L PEG/Asc group, respectively, showed no acute gastropathy related to bowel cleansing agents (score 0), while 58.2% and 83.3% in the middle-aged group, and 58.5% and 82.6% in the old-aged group showed no acute gastropathy related to bowel cleansing agents (score 0), respectively. Among those with acute gastropathy, the severity was mainly indicated by a LANZA score of 3 (3–10 erosions). The percentage of patients with acute gastropathy in the OST and 1-L PEG/Asc groups were 38.6% and 9.1%, 35.8% and 14.0%, and 36.9% and 15.1% in the young, middle-aged, and old-aged groups, respectively.

3. Efficacy of preparation according to age groups

Table 3 shows the bowel preparation efficacy and colonoscopy outcomes according to age group. Successful cleansing

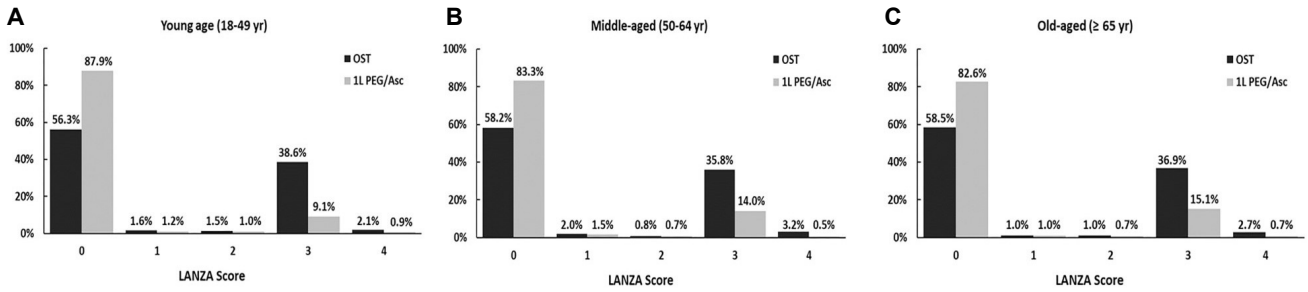

Fig. 2. The severity of gastric mucosal injury based on LANZA scores in patients taking bowel-cleansing agents according to age groups: (A) young age (18–49 years), (B) middle-aged (50–64 years), and (C) old-aged (≥65 years). OST, oral sulfate tablet; PEG/Asc, polyethylene glycol with ascorbate.

Table 3. Bowel Preparation Efficacy and Colonoscopy Outcomes According to Age

Preparation efficacy and colonoscopy outcomes	Young age (18–49 years) (n=1,758)	Middle-aged (50–64 years) (n=2,241)	Old-aged (≥65 years) (n=712)	p-value
Boston Bowel-Preparation Scale				
Total score	7.9±1.5[b]	7.8±1.5[c]	7.7±1.6[b,c]	0.007
Successful cleansing (all segments ≥2)	1,618 (92.0)	2,080 (92.8)	647 (90.9)	0.223
High-quality cleansing (all segments =3)	955 (54.3)[b]	1,165 (52.0)[c]	340 (47.8)[b,c]	0.012
High-quality cleansing in each segment				
Right-sided colon	1,020 (58.0)[b]	1,262 (56.3)[c]	371 (52.1)[b,c]	0.027
Transverse colon	1,430 (81.3)[a,b]	1,752 (78.2)[a,c]	530 (74.4)[b,c]	<0.001
Left-sided colon	1,129 (64.2)[a,b]	1,360 (60.7)[a]	408 (57.3)[b]	0.003
Colonoscopy outcomes				
Polyp detection rate	760 (43.2)[a,b]	1,314 (58.6)[a,c]	492 (69.1)[b,c]	<0.001
Adenoma detection rate	420 (23.9)[a,b]	869 (38.8)[a,c]	362 (50.8)[b,c]	<0.001
CRC detection rate	0 (0.0)	0 (0.0)	4 (0.6)	NA

Values are presented as mean±standard deviation or number (%).
CRC, colorectal cancer; NA, not available.
Superscripts denote p<0.05: [a]between the young and middle-aged groups; [b]between the young and old-aged groups; and [c]between the middle and old-aged groups.

was observed in ≥90% of the patients in all age groups. However, the total BBPS score and high-quality cleansing were significantly lower in the old-aged group than in the other age groups (p=0.007 and p=0.012, respectively). Moreover, high-quality cleansing in each segment was also lower in the old-aged group than in the other age groups (all p<0.05), while the PDR and ADR were significantly higher in the old-aged group than in the other groups (both p<0.001).

Table 4 shows the bowel preparation efficacy and colonoscopy outcomes according to cleansing agents in each age group. In the young age group, the total BBPS score was significantly higher in the OST group than in the 1-L PEG/Asc group (p=0.034); however, this was not different between the OST and 1-L PEG/Asc groups in the other age groups. Furthermore, in all age groups, successful and high-quality cleansing of each segment did not differ significantly between the OST and 1-L PEG/Asc groups. Notably, in the young age group, the PDR was significantly higher in the OST group than in the 1-L PEG/Asc group (p<0.001); however, in the other age groups, this was not different between the OST and 1-L PEG/Asc groups. Moreover, the ADR and CRC detection rates did not differ between the OST and 1-L PEG/Asc groups in any age group.

4. Laboratory profiles

The laboratory profiles of the study population on the day of the colonoscopy are shown in Table 5. Although most laboratory results remained within the normal ranges, all age groups showed significant differences between the OST and 1-L PEG/Asc group in all laboratory values after taking bowel

Table 4. Bowel Preparation Efficacy and Colonoscopy Outcomes According to Age Group and Preparation Agent

Preparation efficacy and colonoscopy outcomes	Young age (18–49 years) (n=1,758)			Middle-aged (50–64 years) (n=2,241)			Old-aged (≥65 years) (n=712)		
	OST (n=822)	1-L PEG/Asc (n=936)	p-value	OST (n=1,422)	1-L PEG/Asc (n=819)	p-value	OST (n=407)	1-L PEG/Asc (n = 305)	p-value
Boston Bowel-Preparation Scale									
Total score	8.0±1.5	7.8±1.6	0.034	7.9±1.5	7.8±1.5	0.635	7.7±1.6	7.7±1.6	0.749
Successful cleansing (all segments ≥2)	760 (92.5)	858 (91.7)	0.541	1,318 (92.7)	762 (93.0)	0.755	368 (90.4)	279 (91.5)	0.628
High-quality cleansing (all segments =3)	464 (56.4)	491 (52.5)	0.094	741 (52.1)	424 (51.8)	0.877	193 (47.4)	147 (48.2)	0.837
High-quality cleansing in each segment									
Right-sided colon	497 (60.5)	523 (55.9)	0.052	806 (56.7)	456 (55.7)	0.645	211 (51.8)	160 (52.5)	0.871
Transverse colon	683 (83.1)	747 (79.8)	0.078	1,118 (78.6)	634 (77.4)	0.504	299 (73.5)	231 (75.7)	0.491
Left-sided colon	547 (66.5)	582 (62.2)	0.057	865 (60.8)	495 (60.4)	0.855	232 (57.0)	176 (57.7)	0.851
Colonoscopy outcomes									
Polyp detection rate	393 (47.8)	367 (39.2)	<0.001	840 (59.1)	474 (57.9)	0.580	277 (68.1)	215 (70.5)	0.487
Adenoma detection rate	213 (25.9)	207 (22.1)	0.062	558 (39.2)	311 (38.0)	0.553	199 (48.9)	163 (53.4)	0.230
CRC detection rate	0 (0.0)	0 (0.0)	NA	0 (0.0)	0 (0.0)	NA	3 (0.7)	1 (0.3)	0.639

Values are presented as mean±standard deviation or number (%).
CRC, colorectal cancer; NA, not available; OST, oral sulfate tablet; PEG/Asc, polyethylene glycol with ascorbate.

Table 5. Laboratory Parameters on the Day of the Colonoscopy According to Age Group and Preparation Agent

Laboratory parameter	Young age (18–49 years) (n=1,758)			Middle-aged (50–64 years) (n=2,241)			Old-aged (≥65 years) (n=712)		
	OST (n=822)	1-L PEG/Asc (n=936)	p-value	OST (n=1,422)	1-L PEG/Asc (n=819)	p-value	OST (n=407)	1-L PEG/Asc (n=305)	p-value
BUN (mg/dL, Ref 6–20)	11.3±3.1	13.1±3.2	<0.001	13.0±3.8	15.5±4.4	<0.001	14.2±3.9	17.5±5.0	<0.001
Sodium (mEq/L, Ref 136–145)	140.4±2.4	140.9±2.1	<0.001	140.9±2.5	142.0±2.3	<0.001	141.1±2.9	143.0±2.7	<0.001
Potassium (mEq/L, Ref 3.5–5.1)	4.4±3.4	4.6±3.8	<0.001	4.4±0.4	4.5±0.4	<0.001	4.4±0.4	4.5±0.4	0.015
Chloride (mEq/L, Ref 98–107)	102.2±2.7	107.9±3.2	<0.001	102.2±2.7	108.9±3.3	<0.001	102.8±3.6	109.6±3.5	<0.001
Calcium (mg/dL, Ref 9.1–10.6)	9.8±0.4	10.0±0.4	<0.001	9.8±0.4	10.1±0.5	<0.001	9.7±0.4	10.0±0.5	<0.001
Phosphorus (mg/dL, Ref 2.5–4.5)	3.4±0.5	4.0±0.5	<0.001	3.5±0.6	4.1±0.7	<0.001	3.5±0.6	4.2±0.7	<0.001

Values are presented as mean±standard deviation.
BUN, blood urea nitrogen; OST, oral sulfate tablet; PEG/Asc, polyethylene glycol with ascorbate; Ref, reference range.

preparation agents. Notably, all laboratory data in the 1-L PEG/Asc group were higher than those in the OST group. As shown in Fig. 3, the differences in the distribution of sodium, chloride, BUN, and phosphate levels between the two bowel preparation agents became more noticeable as age increased; however, the differences in the distribution of potassium were more noticeable in the younger age groups. In contrast, no differences were observed in the distribution of calcium levels according to age.

DISCUSSION

To our knowledge, this large observational study was the first to compare acute gastropathy upon EGD examination according to age in groups taking OST or the 1-L PEG/Asc for bowel preparation. We found that acute gastropathy occurred more often in the OST group than in the 1-L PEG/Asc group across all age groups. Moreover, the difference in the incidence of acute gastropathy between the groups was largest in the young group, followed by the middle-aged and old-aged

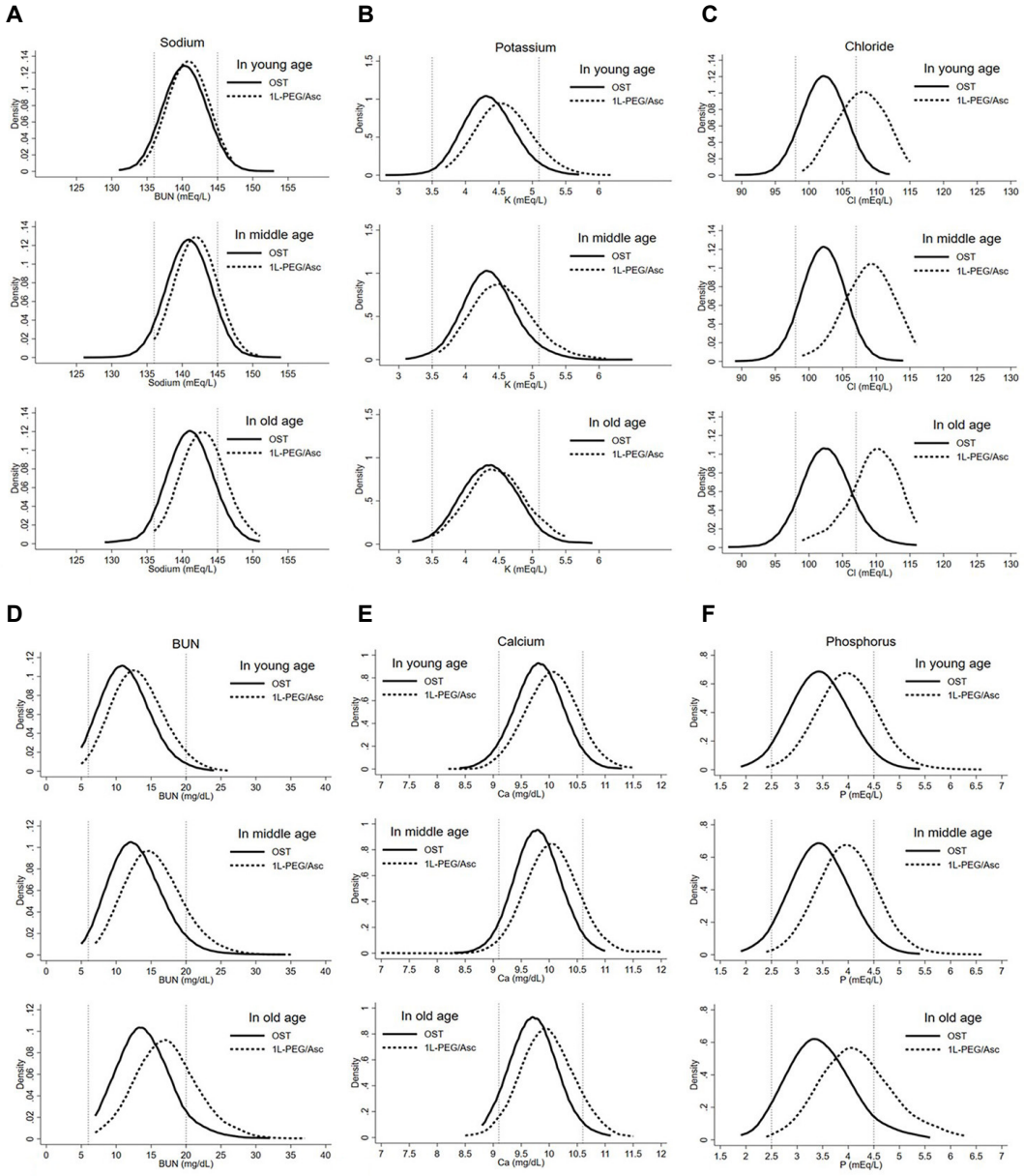

Fig. 3. Distribution of each laboratory parameter on the day of the colonoscopy according to age groups: (A) sodium, (B) potassium, (C) chloride, (D) BUN, (E) calcium, and (F) phosphorus (vertical lines below the graphs' curves indicate the upper and lower limits of normal values). BUN, blood urea nitrogen; OST, oral sulfate tablet; PEG/Asc, polyethylene glycol with ascorbate.

groups. Our results also showed that acute gastropathy associated with OST occurred regardless of age, while that associated with 1-L PEG/Asc occurred more frequently in older age groups, which is consistent with a previous study that reported an age ≥60 years was a risk factor for developing hemorrhagic gastropathy after taking bowel preparation agents.[13] Although OST-related gastropathy has been observed not infrequently, it does not have any particular clinical significance leading to additional medications or treatments.

Acute gastropathy caused by bowel preparation agents is characterized by erosive lesions of the antrum or longitudinal ulcers containing hematin in the stomach.[15,16] It is commonly found in portions dependent on gravity, such as the GC and posterior wall of the stomach.[13,14] Therefore, in this study, acute gastropathy was defined by dividing it into three stages: AGML-like lesions, which represent longitudinally directed ulcers with hematin; erosive lesions; and hyperemia, a milder form than the others. In addition, we classified acute gastropathy according to its location of occurrence – either on the GC side on the body of the stomach or in other location. We found that acute gastropathy occurred more frequently on the GC side than on the lesser curvature side, which was consistent with a previous study showing that most lesions occurred in the GC.[13] In this study, most patients with gastric mucosal injury had a severity score of 3, as measured using the LANZA score, which indicated the presence of 3–10 erosive lesions. In the 1-L PEG/Asc group, the proportion of patients with a severity score of 3 gradually increased with age; however, in the OST group, there was no significant difference in the proportion of patients with a severity score of 3 according to age. There was a significant difference between 1-L PEG/Asc and OST at the most severe point, with a score of 4 indicating deep mucosal injury (ulceration) or more than ten erosive lesions (0.7% vs. 2.5%). However, there were no significant differences between the groups in terms of age.

The mechanism of acute gastropathy caused by the ingestion of a preparation agent remains uncertain. The possible mechanism may be multifactorial and is likely related to the high osmolality of the concentrated solution and the direct thermal effect caused by insufficient dissolution from the ingestion of small amounts of water than the recommended amount of water in the instructed education.[13-15] Speculation regarding this cause might explain the results of our study showing that the OST group (tablet type), which is likely to be partially dissolved, suffered more gastric mucosal injury than the solution-type group. In a real-world experience, OST-related gastropathy is observed more frequently in patients who drink less water than the instructed education. Therefore, we could instruct subjects to drink about 250–500 mL of water before starting OST medications (pre-dosing) in order to prevent OST-related gastropathy

Aspirin or other NSAIDs are generally considered to be more likely to trigger acute gastric mucosal injury.[24] However, a previous study showed that the chronic use of aspirin had no effect on hemorrhagic gastropathy after bowel preparation, which is consistent with some of our findings.[13] In our study, the proportions of patients taking antiplatelet agents or NSAIDs in the young, middle-, and old-aged groups were 2.7%, 11.0%, and 28.6%, respectively. However, the proportions of the AGML-like lesions were 16.3%, 17.7%, and 17.9% in the OST group and 3.3%, 6.2%, and 5.2% in the 1-L PEG/Asc group, respectively. This indicates that the AGML-like lesions found in our study were more related to bowel preparation agents than to ulcerogenic drugs.

The incidence of nausea, vomiting, abdominal discomfort, and abdominal pain, which are gastrointestinal symptoms likely associated with acute gastropathy, appear to differ from the rate of acute gastropathy observed upon EGD. These results suggest that acute gastropathy upon EGD examination after the administration of bowel preparation agents may not cause clinically significant discomfort. In previous animal-model research using pigs, the macro- and microscopic acute gastric mucosal injury induced by bowel cleansing agents was characterized by the superficial nature, and spontaneous reversibility with healing occurring in ≤72 hours.[25,26] Regarding clinical safety, nausea and vomiting were significantly higher in the OST group than in the PEG/Asc group; however, in contrast, a previous study reported higher nausea and vomiting in the PEG/Asc group than in the OST group.[8,9] In our study, the OST group had higher rates of acute gastropathy observed upon EGD than the 1-L PEG/Asc group (42.3% vs. 14.7%, $p<0.001$). Therefore, the more frequent gastrointestinal symptoms in the PEG/Asc group may be due to the disgusting odor or taste of the concentrated agents and the high dose of ascorbate rather than due to acute gastropathy.[24] It is supported by previous findings that 1-L PEG/Asc contains 40.6 g of ascorbate causing more abdominal discomfort, bloating, nausea, and vomiting than 2-L PEG/Asc containing 9.4 g ascor-

bate (34.6% vs. 18.4%, p=0.003).[27] Conversely, the gastrointestinal symptoms in the OST group may have occurred because the subjects consumed more accessible tasteless tablets and less free water than necessary.

Notably, the middle- and old-aged groups often chose OST due to the tasteless nature of the tablet formation in contrast to the unpleasant taste and smell they experienced while consuming bowel cleansing agents in solution form during a previous colonoscopy. However, younger age groups might have chosen 1-L PEG/Asc because they have no previous experience with liquid preparation agents and prefer the less expensive solution form, which is one-fifth the price of the OST in our country. In previous studies comparing the effectiveness and safety of OST and low-volume PEG/Asc, satisfaction with taste or smell was higher for OST, and the proportion of subjects willing to use the same agent in the next colonoscopy was also significantly higher for OST.[8,9] These results suggest that the proportion of patients who choose tablet forms of bowel preparation agents will increase. Furthermore, as this form may be preferred by the elderly, research on the safety of its use in the elderly may become significant.[10]

In this study, we found that the OST group had a significantly better bowel preparation effect than the 1-L PEG/Asc group in the young age group; however, there was no difference between these two groups in the middle- and old-aged groups, which is consistent with previous studies reporting no difference in BBPS between OST and 1-L PEG/Asc in 28 patients aged ≥65 years.[9] One previous study comparing 2-L PEG/Asc and OST also reported no difference in the bowel cleansing effect in people aged >65, whereas OST had a significantly better bowel preparation effect than 2-L PEG/Asc in patients aged ≤65 years, similar to our study.[10] Another study comparing OST and 1-L PEG/Asc showed that the bowel preparation effect of OST was superior, especially in the right colon, at all ages.[8]

Our results regarding the distribution of each laboratory parameter are consistent with those of previous studies. Patients who took OST or 1-L PEG/Asc commonly had decreased BUN, calcium, phosphate, and potassium and increased sodium; however, changes in chloride and phosphate levels had different patterns between the OST and 1-L PEG/Asc groups.[8,28] Therefore, the distribution of chloride and phosphate values between the two groups shows a more apparent difference than other parameters like the results in this study. We also found that the differences in sodium, chloride, BUN, and phosphate between the OST and PEG groups increased with age, while that for potassium increased with a younger age. Moreover, there was no difference in the distribution of calcium between the groups according to age. In contrast, Di Palma et al.[8] reported that all parameters showed no significant difference between elderly and non-elderly groups. This might be due to their smaller number of study participants than that in our study, and their numbers may therefore not reach statistical significance for subgroup analysis by age. Other previous studies have stated that most changes in laboratory values after taking bowel preparation agents tended to be tolerable and rarely clinically meaningful.[8,9,28,29] In this study, we found that the shift of the laboratory parameters' distribution after taking 1-L PEG/Asc was more outside the normal range than that with OST, and this was more pronounced in older groups. Therefore, the use of 1-L PEG may raise concerns regarding the risk of more hypernatremia and electrolyte shifting.[30] Additional large-scale prospective studies are necessary to check electrolyte changes observed in this study, as our finding is limited by an observational study design.

This study had some limitations. First, this retrospective study did not collect dietary habits, all medication history, and lifestyle patterns, which may be associated with the occurrence of gastropathy. Considering that AGML-like erosion or ulcer is extremely rare in EGD performed on healthy, asymptomatic subjects, these findings were classified as OST-related gastropathy in our study. Even though, we could not collect all medication history, we collected ulcerogenic medication history, such as antiplatelet agent, anticoagulant, and non-steroidal anti-inflammatory drug. However, a prospective study is mandatory to control all these risk factors. Second, OST-related gastropathy may be influenced by drug compliance, water intake, and timing of administration, which could not be controlled in a real-world practice. Therefore, a prospective study controlling these variables are necessary. Third, our results might not be generalizable because a healthy population undergoing colonoscopy and EGD for screening may indicate a selective bias. Fourth, due to the retrospective nature of health check-up in our study, we could not survey satisfaction after taking bowel preparation agents, or symptoms correlated with acute gastropathy due to a lack of follow-up at the clinic. Finally, we were only able to conduct laboratory tests after bowel preparation; therefore, we were unable to compare the changes in laboratory parameters before and after bowel preparation.

In conclusion, acute gastropathy was more strongly associated with OST than with 1-L PEG/Asc during bowel preparation in all age groups. Therefore, physicians should take acute gastropathy associated with low-volume agents into consideration during bowel preparation for all age groups.

AUTHOR CONTRIBUTIONS

CJM and YJY were involved in the study concept and design and drafted the manuscript. KMS, PSB and LMH contributed to the analysis and figure. KMS and PSB supervised the data collection. CJM and YJY critically revised the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

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