Original Article

Comparison of Gastric Residual Volume and pH between Single and Split-Dose Bowel Preparation in Patients Undergoing Esophago-Gastro-Duodenoscopy and Colonoscopy: A Randomized Controlled Trial

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Background: Colonoscopy is an effective surveillance for the diagnosis and screening of colorectal cancer (CRC). Prior to the procedure, people would take laxatives for a good visualization of bowel texture. Although a split-dose bowel preparation has become popular, many anesthesiologists are concerned about pulmonary aspiration.

Objective: To study the gastric residual volume and pH in patients taking split-dose bowel preparation as compared to those having laxatives on the day before the procedure.

Materials and Methods: One hundred patients were randomized equally into two groups, as A for a single-dose, and B for a split-dose regimen. All patients underwent endoscopy under standard anesthetic care. The total gastric residual volume was suctioned, and pH was measured through the endoscope. The surgical team was unaware of the study protocol. The quality of bowel cleansing was assessed by the endoscopist using the Boston Bowel Preparation Scale (BBPS).

Results: The bowel cleansing, the latency period, the endoscopist and patients' satisfaction of single-and split-dose group were 7.06±1.4 and 8.14±1.1, 13.3±1.1 and 4.2±0.4 hours, 62.0% and 94.0%, and 90.0% and 74.0%, respectively. They all showed statistically significant differences between the two groups ($p<0.05$).

Conclusion: The gastric residual volume and pH were not different between the split and single-dose preparations. Therefore, it might not increase the risk of aspiration pneumonitis. However, the split-dose technique was more effective in colon cleansing, patients' tolerability, acceptability, and compliance than the preparations administered entirely the day or evening before the surgical procedure.

Keywords: Gastro-colonoscopy; Single-dose bowel preparation; Split-dose bowel preparation; Gastric residual volume; Anesthesia

Received 15 March 2021 | Revised 31 August 2021 | Accepted 2 September 2021

J Med Assoc Thai 2021;104(10):1597-603

Website: http://www.jmatonline.com

Colorectal cancer (CRC), as a life-threatening disease, is the third most common cancer in males and the fifth in females in Thailand[1]. Today, colonoscopy, a procedure without morbidity or mortality, is an effective surveillance for the diagnosis and screening of CRC particularly in people aged over 50[2].

The scheduling of people receiving colonoscopy needs proper management under a provisional protocol. Essentially, patients must take soft food followed by a clear fluid diet for a few days. In addition, they are required to take laxatives for bowel cleansing before the time of the procedure. This is for the good visualization of bowel texture during the endoscopic maneuver, lessening of the procedure time and relieving patient's discomfort.

Colon cleansing preparations are broadly classified into three groups. First, osmotic laxatives including agents such as sodium phosphate (NaP), magnesium citrate, and mannitol, are the most common. These increase colon water content by

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How to cite this article:

Ongiem A, Kaosombatwattana U, Katseesung P, Udompunthurak S, Vichitvejpaisal P. Comparison of Gastric Residual Volume and pH between Single and Split-Dose Bowel Preparation in Patients Undergoing Esophago-Gastro-Duodenoscopy and Colonoscopy: A Randomized Controlled Trial. J Med Assoc Thai 2021;104:1597-603.

doi.org/10.35755/jmedassocthai.2021.10.12688

attracting extracellular fluid efflux through the bowel wall and maintaining oral fluids in the lumen. Second, polyethylene glycol (PEG), a high molecular weight non-absorbable macrogol polymer, is now broadly used as a colon cleansing preparation. As a result of the osmotic effect of the polymer, the electrolyte solution is retained in the colon, where it acts as a bowel cleanser[3].

Available data suggest that NaP achieves excellent cleansing when the first dose is administered the day before the examination and the second one a few hours before the colonoscopy. This is known as a split-dose bowel preparation. On the other hand, PEG administered on the same day renders a better preparation quality than when given the day before[4-7].

Nevertheless, many anesthesiologists are concerned about the possible aspiration of gastric residual fluid when a last dose is taken close to the commencement of anesthesia. Therefore, a standard practice in many institutions is to require a waiting time of six to eight hours before the start of anesthesia after the last ingestion of a bowel preparation agent[8].

As a result, investigators would like to find out the gastric residual volume in patients taking split-dose bowel preparation as compared to those having laxatives on the day before colonoscopy. Gastric residual volume is the amount of liquid consists mainly of drinking laxative or water, and secreted gastrointestinal juice.

Materials and Methods

After the Siriraj Institutional Review Board approval (COA No. Si 236/2019), the study was registered on the Thai Clinical Trial Registry (TCTR20191113001) and written informed consent forms were obtained from all subjects. This prospective study was performed from October to December 2019.

Inclusion criteria were elective patients, aged between 18 and 70 years old, meeting the American Society of Anesthesiologists (ASA) class I-II, undergoing elective, gastro-colonoscopy under general anesthesia at Siriraj GI Endoscopy Center, Siriraj Hospital.

Exclusion criteria were patients with ASA class greater than III, inability to understand informed written consent, dysphagia, gastric outlet obstruction, previous gastric or duodenal surgery, and cardiovascular or end-stage renal diseases.

Withdrawal criteria were patients who were unhappy to continue under the study protocol and those with unstable vital signs or procedural failure.

The study was designed with the significance of 5% and 90% power to the test, as well as a hypothesis that a split-dose bowel preparation was non-inferior to a single-dose bowel preparation. According to published studies, the true difference in mean of the gastric residual volume between single and split-dose bowel preparation groups was 0 mL with the common standard deviation of 16 mL. If this was the gastric residual volume, a non-inferiority margin fixed at 10 mL, then the targeted recruitment was 45 patients per group. The 10% was added to the cohort to accommodate dropouts creating a population size of 100 participants.

On the day of counseling

A co-researcher invited patients to participate and explained the project in detail. All participants were randomized using Block of Four 25 blocks into two groups, Group A, the single-dose group, where patients had PEG three liters between six and eight p.m. on the day before surgery, and Group B, the split-dose group, where patients had PEG two liters between six and eight p.m. on the day before surgery and one liter between three and five 5 a.m. on the day of the procedure.

On the day of colonoscopy

A co-researcher interviewed all participants regarding laxative ingestion and fluid intake in the waiting room. Then a nurse moved the patient into the operating room where a nurse anesthetist manipulated the patient with standard monitoring, namely electrocardiogram (EKG), percutaneous oxygen saturation (SpO_2), and non-invasive blood pressure (NIBP). After placing the patient in the left lateral position, an anesthetist administered intravenous fentanyl and propofol for deep sedation. The gastric residual fluid was suctioned and collected in a fluid container that was attached to the endoscope just before the esophago-gastro-duodenoscopy. The gastric residual volume was measured, and pH was verified using a pH meter (Hanna HI98103, USA).

At the end of the colonoscopy, the board-certified endoscopist who had at least 10-year experience and was unaware of the techniques, assessed the quality of bowel cleansing by the Boston Bowel Preparation Scale (BBPS) where 0 was poor and 9 was entirely clean. Though the BBPS of 5 or greater was the endpoint for the adequacy of bowel preparation, most endoscopists and investigators agreed to accept the BBPS of greater than 6[9]. Additionally, the endoscopist and patients' satisfaction were

Table 1. Patients' demographic characteristics

Variables	Single-dose (n=50); mean±SD	Split-dose (n=50); mean±SD	p-value [95% CI]
Age (year)	55.9±10.5	54.6±9.9	0.520
BMI (kg/m^2)	24.5±4.2	23.7±3.4	0.300
Sex male:female	13:37	15:35	0.656
ASA I:II	20:30	22:28	0.685
Underlying diseases			
Diabetes mellitus	6	8	0.564
Hypertension	16	13	0.509
Dyslipidemia	16	12	0.373
Latency period			
Clear fluid diet (hour)	17.0±2.6	17.0±2.6	0.9
Laxative (hour)	13.3±1.1	4.2±0.4	<0.001*
Parameters			
Gastric residual volume (mL)	17.9±16.1	15.3±13.1	0.4 [–3.29 to 8.35]
pH	1.35±0.6	1.25±0.5	0.4 [–0.11 to 0.31]
BBPS	7.06±1.4	8.14±1.1	<0.001* [–1.58 to –0.58]
Satisfaction score			
Endoscopist	62.0%	94.0%	<0.001*
Patients	90.0%	74.0%	0.04*

ASA=American Society of Anesthesiology; BBPS=Boston bowel preparation score; BMI=body mass index; CI=confidence interval; SD=standard deviation

* p<0.05 significance, a 95% CI for difference between single- and split-dose

assessed by using 10 numeric rating scale with 1 as not satisfied, 5 as fair, and 10 as strongly satisfied.

Statistical analysis

Data analysis was performed under the PASW Statistics for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA). All parameters were expressed by percentage, mean and standard deviation. A comparison between the two groups was determined by an independent t-test. Categorical data were assessed by the chi-square test or the Fisher's exact test. Spearman rank correlation was analyzed for the relationship between the latency period (the time between the last laxative and the commencement of endoscopy), gastric residual volume, pH, and the quality of bowel preparation. A p-value of less than 0.05 was considered as a statistically significant difference at the 0.95 confidence interval.

Results

One hundred patients participated in the present study without any procedure-related adverse events such as pulmonary aspiration or oxygen desaturation. Patients' demographic characteristics were comparable between the two groups. They were 28 (28%) male, 72 (72%) female with an age of 55±10.2, and ASA I 42 (42%) and II 58 (58%) (Table 1).

The BBPS, the latency period, and the endoscopist and patients' satisfaction score of the single- and the split-dose group were 7.06±1.4 and 8.14±1.1, 13.3±1.1 and 4.2±0.4 hours, 62.0% and 94.0%, and 90.0 and 74.0%, respectively. They all showed statistically significant differences (p<0.001) (Table 1).

However, the latency period, the gastric residual volume, and the pH of the single- and the split-dose group were 17.0±2.6 and 17.0±2.6 hours, 17.9±16.1 and 15.3±13.1 mL, and 1.35±0.6 and 1.25±0.5, respectively. There appeared to be no differences as p-values were 0.9, 0.4, and 0.4, correspondingly (Table 1).

Additionally, there was a correlation between the latency period to the quality of bowel preparation (p<0.001) but not to the gastric residual volume (p=0.869) and pH (p=0.444) (Table 2).

Discussion

The gastric residual volume and pH in one hundred patients having single- or split-dose bowel preparations before esophago-gastro-duodenoscopy and colonoscopy were compared. The split-dose group showed superiority with bowel cleansing, latency

Table 2. Correlation between the latency period to gastric residual volume, pH, and quality of bowel preparation

Variables	Latency period	
	Spearman's correlation coefficient (r)	p-value
Gastric residual volume	0.017	0.869
pH	0.080	0.444
Bowel quality	–0.361	<0.001*

* p<0.05 significance

period, plus endoscopist and patient satisfaction than the single-dose group. Additionally, there was a correlation between the latency period to the quality of bowel cleansing, but not to gastric residual volume and pH.

By and large, anesthesia personnel are highly concerned about intraoperative aspirated pneumonitis known as Mendelson's syndrome, since the regurgitation of stomach contents across the lower respiratory tract can cause inflammation of the lung tissue. The situation is aggravated by decreased gastric pH and increased gastric residual volumes with a pH of less than 2.5 and volume more than 0.4 mL/kg, including a full stomach, or delayed gastric emptying time[10]. However, the present study revealed that pulmonary aspiration might rarely happen in the split-dose bowel preparation as compared to the single-dose regimen for endoscopy.

This was supported by many previous studies. Huffman et al (2010)[11] in an observational study on split-dose bowel preparation for colonoscopy and gastric residual fluid volume at a tertiary care hospital-based endoscopy unit stated that the range of gastric residual volume in patients receiving split-dose bowel preparation was not different from that in patients receiving bowel preparation the evening before the procedure. Prieto-Frias et al (2016)[12] in a single-center observational study on split-dose sodium picosulfate-magnesium citrate colonoscopy preparation confirmed that the split-dose technique achieved lower gastric residual volume. Agrawal et al (2016)[13] in a prospective observational study on gastric residual volume after a split-dose preparation compared with an evening-before polyethylene glycol bowel preparation also concluded that the residual volume and the risk of aspiration were identical after either preparation technique, and the sedative anesthesia was safe to be administered two hours after bowel preparation.

Additionally, Alghamry et al (2017)[14] in a study on split-dose bowel preparation with polyethylene glycol for colonoscopy performed under propofol sedation stated that the consumption of the bowel preparation agent within three to four hours before anesthesia resulted in a similar gastric residual volume and pH as those achieved by more prolonged fasting, with no increased risk of aspiration even in patients perceived to be at high risk. Xue et al (2017)[8] , in a prospective observational study on gastric residual volume after split-dose bowel preparation versus conventional single-dose regimen before anesthetic colonoscopy and using the BBPS for bowel cleansing quality assessment summarized that the gastric residual volume and the risk of aspiration after a split-dose preparation were comparable with that after a conventional technique. In addition, Cheng et al (2017)[15] in a prospective observational study on gastric residual volume after bowel preparation with polyethylene glycol for elective colonoscopy claimed that patients with latency periods of less or more than three hours had indifference in residual volume. However, patients with the same-day preparation showed mild, clinical insignificant increases of volume as compared to the split-dose technique.

Furthermore, Sriphongphankul et al (2019)[16] in a pilot study of a randomized controlled trial on a split-dose versus full a single-dose regimen of polyethylene glycol for bowel preparation in pediatric colonoscopy showed that the split-dose technique with an electrolyte solution for bowel preparation revealed superior efficacy, potential tolerability, and acceptability as compared to the traditional full single-dose regimen.

Interestingly, the correlation between the latency period to the quality of bowel cleansing, but not to gastric residual volume and pH implied that the split-dose bowel preparation was superior in clinical practice because of the shorter latency period, the better cleansing and anesthetic guidelines considering that gastric residual fluid was independent of clear liquid fasting. This was supported by Bucci et al (2014)[17] in a series of meta-analyses of controlled studies on optimal bowel cleansing for colonoscopy that concluded that the split-dose regimen was superior and had a higher compliance than that of the non-split-dose method particularly on the runway time or the interval time between the last drink of purgative and the beginning of the colonoscopy, where the longer, the worse the cleansing. In addition, Bucci et al (2019)[18] in a systematic review with meta-analysis titled same-day regimen as an alternative to split preparation for colonoscopy summarized that both techniques had an adequate cleansing. However, the

split-dose procedure obtained a better cleansing rate with polyethylene glycol.

Likewise, Prieto-Frias et al (2016)[12] in a single-center observational study on split-dose sodium picosulfate-magnesium citrate colonoscopy preparation confirmed that the split-dose technique achieved a higher cleansing effectiveness than a previous-day regimen.

Martel et al (2015)[19] in a meta-analysis on split-dose preparations found they were superior to day-before bowel cleansing regimens than split-dose regimens. They increased the quality of colon cleansing and were preferred by patients compared with day-before preparations. Similarly, Chiu et al (2006)[20] in a prospective endoscopist-blinded randomized trial on the impact of colon preparation timing on colonoscopic detection of colorectal neoplasms concluded that the preparation on the day of procedure had a better cleansing quality and higher diagnostic yield than that of the night before.

However, Huffman et al (2010)[11] in an observational study on split-dose bowel preparation for colonoscopy and gastric residual fluid volume at a tertiary care hospital-based endoscopy unit stated that there was no association between the interval from the last actual fluid ingestion and procedure start time and the gastric residual volume in the split-dose preparation group.

Regarding the endoscopist's and patient's satisfaction on the split-dose bowel regimen, it seemed to agree with de Miranda Neto et al (2020)[21] in an evidence-based review on the efficacy and patient tolerability of split-dose sodium picosulfate and magnesium citrate oral solution compared to the polyethylene glycol solution for bowel preparation in outpatient colonoscopy concluded that split-dose regimens were both adequate and safe for bowel preparation for outpatient colonoscopy, with sodium picosulfate and magnesium citrate being more tolerable for patients. In addition, Perreault et al (2018)[22] in a cross-sectional, dual-center study on split versus single-dose preparation tolerability in a multiethnic population concluded that a split-dose bowel preparation was significantly more tolerable and associated with less severe gastrointestinal symptoms than a single-dose preparation. Menees et al (2018)[23] in a retrospective study on how a split-dose bowel preparation improved the adequacy of bowel preparation and gastroenterologists' adherence to guideline recommendations summarized that the split-dose regimen increased endoscopists' compliance to guidelines in average-risk patients with normal colonoscopy. Besides, Kilgore et al (2011)[7] in a meta-analysis of randomized controlled trials on bowel preparation with split-dose polyethylene glycol before colonoscopy stated that the use of a split-dose bowel preparation significantly improved patient satisfaction, increased patient compliance, and decreased nausea.

However, Shah et al (2014)[24] in a prospective randomized study on the comparison of split-dosing versus non-split (morning) dosing regimen for the assessment of quality of bowel preparation for colonoscopy stated that morning preparation might be more convenient for the patient. In addition, Bucci et al (2019)[18] in their systematic review with meta-analysis summarized that patients with split-dose preparation for colonoscopy were more compliant and had less nausea and vomiting but more sleep disturbance than that of the same-day regimen.

Conclusion

The gastric residual volume and pH were not different between the split and the single-dose preparation. Therefore, it might not increase the risk of aspiration pneumonitis. However, the split-dose technique was more effective in colon cleansing, patients' tolerability, acceptability, and compliance than preparations administered entirely the day or evening before the surgical procedure.

Limitation

The present project was conducted at a single center, tertiary care hospital-based endoscopy. Additionally, this non-inferiority trial with high expected event rate (margin) implied a limited number of participants.

What is already known on this topic?

Though a split-dose bowel preparation has become popular for gastro-colonoscopy amongst surgeons and patients, most anesthesiologists still much concerned about pulmonary aspiration.

What this study adds?

According to the criteria of aspiration pneumonitis, the 4-hour latency period was appropriate for patients having a split-dose bowel preparation to gastro-colonoscopy under total intravenous anesthesia.

Funding disclosure

The present research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflicts of interest

The authors declare no conflict of interest.

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