

## Colonoscopy Preparation: Efficacy and Efficiency of Hospital-made Polyethylene Glycol (PEG) Compared with Commercial PEG

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### ABSTRACT

**AIM:** Colorectal cancer is the third most deadly cancer worldwide, and colonoscopy is an effective method for screening for this cancer. Reducing the cost of colonoscopy could help increase adherence of patients with indications for this disease. The aim of this study was to compare the efficacy and cost-effectiveness for bowel clearance between hospital-made polyethylene glycol and the commercial product.

**METHODS:** A simple randomized double-blind study was conducted of 154 patients who underwent colonoscopy from August 2013 to November 2013. The patients were divided into two groups: group A (77 patients) received hospital-made polyethylene glycol prepared by the Pharmacy Department in Cipto Mangunkusumo National General Hospital, and group B (77 patients) received commercial product. The efficacy of bowel clearance in patients was assessed using Aronchick's criteria. The cost-effectiveness was analyzed by comparing the costs between the two products.

**RESULTS:** The quality of bowel clearance did not differ between the two groups ( $P=0.997$ ). In group A, bowel clearance was categorized

as excellent in 32 patients (42%), good in 27 (35.1%), fair in 12 (15.6%), poor in five (6.5%), and inadequate in one (1.3%). In group B, the respective bowel clearance categorizations were 37 (48.1%), 22 (28.6%), 16 (20.8%), two (2.6%), and zero. The production costs per unit were equivalent to 1 United States Dollar for hospital-made polyethylene glycol and 18.2 United States Dollars for commercial product.

**CONCLUSIONS:** The efficacy of bowel clearance did not differ between the two products. Hospital-made polyethylene glycol was more cost-effective than commercial product.

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**Key words:** Colorectal neoplasms; Bowel preparation solutions; Cost-effectiveness; Polyethylene glycol

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### INTRODUCTION

Colorectal cancer is the third most commonly diagnosed cancer and the third leading cause of cancer death. The American Cancer Society has noted that the mortality rate of colorectal cancer could be reduced by prevention by screening for the early detection of colorectal cancer<sup>[1]</sup>. Colonoscopy is considered the most effective colorectal cancer screening method<sup>[2]</sup>. Colonoscopy provides complete visualization of the entire colon, detection and removal of polyps, and diagnostic sampling of cancers. All of these actions can be performed efficiently during the examination<sup>[2,3]</sup>.

The sensitivity of colonoscopy for diagnosing colon cancer is thought to be greater than 90%<sup>[4]</sup>. The diagnostic accuracy of colonoscopy depends upon the bowel-preparation agent, which is

selected according to efficacy, tolerability, safety, and affordability. Accurate colonoscopy also requires optimal visualization of the entire mucosal surface, which requires adequate bowel cleansing to ensure a high-quality, effective, safe, and complete colonoscopy<sup>[5]</sup>.

A consensus document on bowel preparation before colonoscopy noted that many preparation regimens can be applied<sup>[6]</sup>. The first is a dietary regimen comprising fasting or a diet of low-residue foods and clear liquids for 1 day before the procedure<sup>[6,7]</sup>. This procedure is supported by much evidence<sup>[6]</sup>. The '2-6-8 rule' is recommended by The American Society of Anesthesiologists and provides a timetable for a fasting period of 2 hours after consumption of only clear liquids, 6 hours after a light meal, and 8 hours after a full meal<sup>[7]</sup>. This rule was based on studies that assessed gastric residual volume following variable periods of fasting<sup>[8]</sup>.

The second regimen is the use of enemas such as sodium phosphate enemas to clean out the distal segment of the bowel<sup>[6]</sup>. However, this is not safe for patients with an electrolyte or fluid imbalance; e.g. patients with renal or liver insufficiency, congestive heart failure, or liver failure<sup>[7]</sup>.

The third regimen involves high-volume gut lavage, which is used for colonoscopy preparation, but is poorly tolerated and can induce complications caused by the high volume of fluid introduced into the body<sup>[6]</sup>.

The fourth regimen is rectal pulsed irrigation combined with dietary restriction. In this treatment, the patient receives a 30-minute infusion of warm tap water into the rectum through a rectal tube immediately before the colonoscopy. This regimen has some disadvantages, such as being time consuming and needing a registered nurse to perform the irrigation. Chang *et al* developed this regimen and found no significant differences in bowel-cleansing quality when compared with the fifth regimen, polyethylene glycol (PEG)<sup>[6]</sup>.

The fifth regimen is the use of PEG, which is more effective than other regimens as a bowel-cleansing preparation<sup>[6]</sup>. PEG is a nonabsorbable polymer with high molecular weight that acts as an isosmotic laxative agent. PEG comes as a powder including 125 mmol/L sodium, 40 mmol/L sulfate, 35 mmol/L chlorine, 20 mmol/L bicarbonate, and 10 mmol/L potassium. This powder is diluted in 2-3 L of fluid<sup>[7]</sup>, and this solution cleanses the bowel with minimal fluid and electrolyte shifts<sup>[9]</sup>. PEG is now one of the most commonly used regimens in bowel preparation before colonoscopy in adults in Indonesia.

Bowel preparation before the colonoscopy procedure can cause adverse effects such as electrolyte imbalance, abdominal discomfort, nausea, and vomiting. PEG provides excellent cleansing and is relatively safe for patients with an electrolyte imbalance or fluid changes including those with renal failure, congestive heart failure, or liver disease with ascites. It is also the method of choice for infants and children<sup>[10,11]</sup>. PEG may be used in patients suspected of having inflammatory bowel disease without interfering with the diagnosis<sup>[12]</sup>. In another study, Beck *et al* showed that a PEG preparation provided excellent bowel cleansing in 90%-100% of patients and caused no fluid or electrolyte problems<sup>[13]</sup>.

Even though PEG is recognized as the most tolerated and safe procedure for bowel cleansing, it is sold widely at high cost under various brand names. In 2004, colonoscopy was reimbursed at \$300-\$400 in many centers in the United States, and the additional payment for modest additional costs for anesthesia brought the total cost to \$800-\$900. The high cost of colonoscopy also includes the drugs used in bowel preparation<sup>[14]</sup>.

In Indonesia, the national health insurance covers the cost of the colonoscopy examination for both diagnostic and therapeutic purposes, but not for colorectal screening. Because of the high price of commercial PEG, we have tried to reduce the cost by producing a hospital-made PEG whose quality meets the requirement for good bowel cleansing and is acceptable to most patients.

We conducted a prospective, double-blind, randomized controlled study to analyze the efficacy and efficiency of our hospital-made PEG and to compare it with commercial PEG. We hoped that this could improve the affordability of colonoscopy examination and make it available to more patients.

## METHODS

This study was a randomized double-blind controlled trial to compare the efficacy and efficiency of bowel preparation using hospital-made PEG or commercial PEG. The hospital-made PEG preparation, which is in the form of a powder, was prepared by the Pharmacy Department of Cipto Mangunkusumo National General Hospital, Jakarta, and the commercial PEG was Niflec™, produced by Meiji Indonesian Pharmaceutical Industries. Ethics clearance was given by the Ethics Committee of the Faculty of Medicine, University of Indonesia (registered ethics approval number 243/h2.fl/etik/2013). This committee has been registered as one of the Ethics Review Committees in the Asian and Western Pacific Region.

One hundred fifty-four patients who underwent colonoscopy examination were included in this study. They were randomized into two groups: group A (77 patients) received hospital-made PEG, and group B (77 patients) received commercial PEG. The type of PEG used was not known by the researchers or participants.

This study was conducted from April 2013 to November 2013. Patients were included if they were within the age range of 18-70 years, indicated for colonoscopy, had no contraindications for the use of PEG, and provided informed consent. Any patient with a medical diagnosis such as bowel obstruction, perforation, severe colitis, or toxic megacolon was excluded from the study. Patients who consumed <75% or 1,500 mL of the PEG solution were excluded.

In this study, we prepared the hospital-made PEG solution and the commercial PEG the same way, and the compounds used to make both preparations were identical. The instructions given to all patients were in accordance with the instructions in the latest American Society for Gastrointestinal Endoscopy guidelines<sup>[9]</sup>. The patients were asked to dilute PEG powder into 2 liters of drinking water, and they were asked to consume that solution during the last 12 hours before the procedure.

SPSS software (v. 21.0; IBM SPSS, Armonk, NY, USA) was used to analyze all data. The efficacy of the hospital-made PEG and commercial PEG was assessed using Aronchick's criteria scoring scale of 1 to 5 points for the entire colon. This scale grades using semi-quantitative descriptors: (1) Excellent: Small volume of clear liquid or >95% of the surface is seen; (2) Good: Large volume of clear liquid covering 5-25% of the surface, but >90% of the surface is seen; (3) Fair: Some semisolid stool that could be suctioned or washed away, but >90% of the surface is seen; (4) Poor: Semisolid stool that could not be suctioned or washed away and <90% of the surface seen; (5) Inadequate: Solid stool that impedes vision. Repeat preparation and colonoscopy are needed<sup>[15,16]</sup>.

## RESULTS

One hundred seventy-nine patients were eligible to participate in this

study and completed the informed consent form. Twenty-five patients were excluded: nine patients were excluded because of obstruction, 10 patients were excluded because of noncompliance with the bowel-preparation procedure, and six patients were excluded because of a comorbidity that was contraindicated for colonoscopy examination such as thrombocytopenia, anemia gravis, severe colitis, or bleeding. After exclusion of these patients, 154 patients were enrolled in this study.

The demographic data from each group were analyzed and are presented in table 1. Most patients were younger than 60 years, were men, were unemployed, and had completed secondary or a higher level of education. The data also showed that the patient’s educational level correlated inversely with the quality of bowel cleansing.

The efficacy of hospital-made PEG and commercial PEG were compared using the Kolmogorov-Smirnov test, and the data are shown in table 2. The quality of bowel clearance did not differ significantly between the two groups ( $P=0.997$ ).

We compared the cost effectiveness of hospital-made PEG and commercial PEG. The price of commercial PEG (Niflec™) was IDR 200,500 (equivalent to USD 18.2) per sachet, and the production price of hospital-made PEG was IDR 11,000 (equivalent to USD 1) per sachet.

**Table 1** Demographic characteristics.

Variables	Group A n (%)	Group B n (%)	Total n (%)	P value <sup>1</sup>
Age				0.390
18–60 years	66 (43%)	62 (40.3%)	128 (83.1%)	
≥60 years	11 (7.1%)	15 (9.7%)	26 (16.9%)	
Gender				0.628
Male	42 (27.3%)	39 (25.3%)	81 (52.6%)	
Female	35 (22.7%)	38 (24.7%)	73 (47.4%)	
Occupation				0.105
Employed	39 (25.3%)	29 (18.8%)	68 (44.2%)	
Unemployed	38 (24.7%)	48 (31.2%)	86 (55.8%)	
Education				0.611
None to middle school	28 (18.2%)	25 (16.2%)	53 (34.4%)	
High school or higher level	49 (31.8%)	52 (33.8%)	101 (65.6%)	

<sup>1</sup> Chi-square test

**Table 2** Quality of bowel clearance for the two PEG products.

Group	Aronchick’s criteria				Total	P value <sup>1</sup>
	Excellent	Good	Fair	Inadequate		
Group A <sup>2</sup>						0.997
N	32	27	12	1	77	
%	41.5	35.1	15.6	1.3	100	
Group B <sup>3</sup>						
N	37	22	16	0	77	
%	48.0	28.6	20.8	0	100	
Total						
N	69	49	28	1	154	
%	44.8	31.8	18.2	0.6	100	

<sup>1</sup> Kolmogorov–Smirnov; <sup>2</sup>Group A received hospital-made PEG; <sup>3</sup>Group B received commercial PEG.

## DISCUSSION

Colonoscopy is the most important diagnostic tool and an effective method for colorectal cancer screening because of its high accuracy in detecting initial cancerous lesions, and its use has decreased colorectal cancer incidence<sup>[17]</sup>. The quality of colonoscopy is determined by the ability of the clinician to examine the entire mucosa in the colon and to complete the examination within an optimum time. Adequate bowel preparation is essential before a

colonoscopy because hindrance of the visualization of the colon by fecal material increases the probability of missing a lesion and lengthens the procedure time, which causes patient discomfort<sup>[18]</sup>.

An effective method of bowel cleansing that will ensure patient compliance should improve the effectiveness of the examination and minimize the risk of procedural complications<sup>[19]</sup>. The ideal method of colon cleansing should be fast and safe, and provide proper cleaning with minimal discomfort for the patient<sup>[16]</sup>. Inadequate bowel preparation for colonoscopy can lead to missed lesions, cancellation of the procedure, increased procedural time, and possibly increased complication rate<sup>[18]</sup>.

We compared the demographic data, including age, gender, employment status, and educational level, between groups classified according to our national system of demography classification. The chi-square test showed no differences in these characteristics between groups. This shows that the randomization of the patients in this study was successful.

We assessed whether there was a relationship between any demographic characteristic and the quality of bowel cleansing. A study by Modi *et al* found no relationship between educational background and the quality of bowel preparation<sup>[12]</sup>. In another study by Leibold *et al*, the variables associated with optimal bowel preparation included older age, male gender, inpatient status, and later time of day<sup>[20]</sup>.

The comparison between the efficacy of hospital-made PEG and commercial PEG showed that there was no significant difference between them. We also compared the quality of bowel clearance between hospital-made PEG and commercial PEG, and we found no significant difference. In both groups, an ‘excellent’ result was the most frequent outcome, followed by good, fair, poor, and inadequate, in that order. In addition, the frequencies of each quality rating did not differ significantly between groups.

We have been searching for a more affordable bowel-cleansing product of the same quality as commercial PEG, which led us to conduct this randomized controlled trial. We asked the Pharmacy Department of our hospital to produce PEG solution with the same ingredients, amounts, and flavor as the commercial PEG solution. To prevent bias, we used a double-blind method and provided both PEG products in the same package. The efficacy did not differ between the two PEG products. Therefore, we conclude that the effectiveness of the hospital-made PEG was not inferior to that of the commercial PEG.

The results of our study show that the hospital-made PEG was much less expensive than the commercial PEG, which should make colonoscopy more affordable in Indonesia. A lower price of PEG should improve patient compliance with the procedures and access to colonoscopy examination. This is especially important in Indonesia because, in the outpatient setting, agents for bowel preparation are not covered by national insurance.

PEG is a faster, more effective, and better-tolerated method for bowel cleansing than a restricted diet combined with cathartics, high volume lavage, or mannitol<sup>[7]</sup>. Wexner *et al* reported that the independent predictors of an inadequate colonic preparation included delayed colonoscopy starting time, failure to follow preparation instructions, inpatient status, constipation, and use of tricyclic antidepressants<sup>[6]</sup>. Aoun *et al* suggested that the timing of PEG administration is more important than a restricted dietary regimen in determining the quality of bowel cleansing. In their study, the split-dose PEG (3 L on the night before and 1 L in the morning of the procedure day) administered to patients was as effective and better tolerated than the standard 4 L dose given 1 day before the

colonoscopy procedure<sup>[21]</sup>. Other studies have continued to show that the split-dose PEG regimen is superior to the single-dose regimen<sup>[22]</sup>.

A study of colonoscopy preparation by the American Society for Gastrointestinal Endoscopy (ASGE) reported that isotonic PEG preparations are tolerated better and are thus favored by 90% of patients who had previously used an older method of bowel cleansing before PEG became available<sup>[10]</sup>. Split-dose PEG regimens (2-3 L of fluid during the night before the colonoscopy and 1 L of fluid in the morning on the day of the procedure) are acceptable alternative regimens that increase patient tolerance. The bowel-cleansing process with PEG solution takes 3-4 hours and involves a minimum exchange of fluids and electrolytes<sup>[7]</sup>. In the ASGE study, patients usually ingested the rest of the PEG preparation on the day of the procedure 5 hours before undergoing the colonoscopy. This timeframe improved the quality bowel of cleansing compared with ingestion of the rest of the PEG preparation on the preceding day about 19 hours before the procedure<sup>[10]</sup>. The study by Church also found that PEG consumption <5 hours before the procedure resulted in better preparation for bowel cleansing than when given >19 hours before the procedure<sup>[13]</sup>.

The efficacy of bowel preparation did not differ significantly between hospital-made PEG and commercial PEG, and both PEG products provided a similar quality of bowel clearance. The hospital-made PEG was more cost-effective than the commercial PEG. For bowel preparation before colonoscopy in Indonesia, we recommend the use of hospital-made PEG produced by Cipto Mangunkusumo National General Hospital, Jakarta.

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## CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

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