A Randomized Controlled Trial Comparing Bowel Preparation by Sodium Phosphate Solution 45 ML x2 Doses versus Sodium Phosphate Solution 30 ML x3 Doses in Patients Undergoing Colonoscopy

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Background: *Colonoscopy is common procedure performed for diagnostic or therapeutic colorectal diseases. Good quality mechanical bowel preparation is important for good visualized colonic mucosa. Sodium phosphate solution ingestion is a common mechanical bowel preparation, with low side effects and less tolerability.*

Objective: *The present study was conducted to compare the efficacy and tolerability of mechanical bowel preparation using the split 45 ml x2 doses and 30 ml x3 doses of sodium phosphate solution in patient undergoing colonoscopy.*

Material and Method: *The present study was conducted in Ramathibodi Hospital, Thailand between November 2015 and December 2016. Eighty eligible patients who underwent colonoscopy at our unit were randomized assigned to study group (sodium phosphate 30 ml x3 doses) and control group (sodium phosphate 45 ml x2 doses). The quality of bowel preparation was evaluated by endoscopist and tolerability was recorded from patient's questionnaire.*

Results: *Eighty participants were included in this study; 65 participants were analyzed about quality of bowel preparation and 34 participants were analyzed about tolerability of bowel preparation. There was no statistical difference in patient characteristic, quality of bowel preparation ($p = 0.68$), nausea ($p = 0.73$), vomiting ($p = 1.00$), pain ($p = 0.25$), difficult to eat this solution ($p = 0.07$), amount of feces ($p = 0.20$), time from last dose to last defecation ($p = 0.72$), and frequency of defecation ($p = 0.76$) between the two bowel preparation regimens.*

Conclusions: *The present study demonstrated no difference in quality and tolerability between the 45 ml x2 doses and 30 ml x3 doses of sodium phosphate solution for mechanical bowel preparation in patient undergoing colonoscopy.*

Keywords: *Bowel preparation, Sodium phosphate solution, Colonoscopy*

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Colonoscopy is a common procedure performed for diagnostic or therapeutic colorectal diseases such as colorectal cancer, colonic polyp, and colitis. Good quality mechanical bowel preparation is crucial for good visualized colonic mucosa and successful colonoscopy[1,2].

Mechanical bowel preparation for patient undergoing colonoscopy is aimed for cleaning feces in colon, which are composed of modification of diet and laxative agents, before the procedure. Apart from the quality of bowel preparation, safety and tolerability are in main consideration before selecting the proper bowel preparation regimen. The ideal bowel preparation regimen should be easy to take, cause minimal patient discomfort, and have no adverse side effect. In old patients with chronic kidney disease, heart disease, or cirrhosis patients, improper mechanical bowel preparation may induce severe dehydration, electrolytes imbalance, and abdominal pain[3].

Sodium phosphate solution is a small volume of hyperosmotic laxative that induces an osmotic diarrhea and results in colonic cleansing. The disadvantage of this solution is that there are potential adverse events involved in administration of this solution such as diarrhea, abdominal pain, nausea, and vomiting. Because of its salty taste, it is difficult for the patients to ingest and complete the regimens[4].

In our opinion, splitting doses of sodium phosphate solution resulting in decreasing volume of solution per dose without changing the total dosage

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may decrease side effect and increase tolerability without changing the quality of bowel preparation.

Our study aimed to compare the efficacy and tolerability of mechanical bowel preparation using 45 ml x2 doses and 30 ml x3 doses of sodium phosphate solution in patients undergoing colonoscopy.

Material and Method

Study design and population

We conducted a prospective, single center, parallel-group, and randomized control trial at Ramathibodi Hospital in Thailand between August 2014 and November 2015. The study was approved by the ethics committee in Ramathibodi Hospital. Every patient provided written inform consent before enrollment.

Patients scheduled for elective colonoscopy during the study period were eligible for the study. Additional inclusion criteria were age 20 to 70 years with body weight greater than 40 kgs, able to provide informed consent, and without any chronic kidney disease, heart disease, and cirrhosis.

Enrollment and randomization

Patients undergoing colonoscopy were assessed for eligibility at outpatient department. Block randomization was generated by a computer program. Sealed opaque envelopes labeled with dose of sodium phosphate solution 45 ml x2 doses (Group A) or 30 ml x3 doses (Group B) were prepared and opened after inform consent was signed.

Intervention

After randomization, the detail of the procedure and potential adverse events of colonoscopy was explained to each study participant, together with the instructive paper for mechanical bowel preparation about diet before undergoing colonoscopy, as well as the time and dose of sodium phosphate ingestion (45 ml at 13 and 19 o'clock or 30 ml at 13, 16 and 19 o'clock). In addition, the patient completed the questionnaire about demographic data, tolerability, compliance, and side effect of mechanical bowel preparation. The questionnaire was returned to the colonoscopic room on the day of procedure.

Colonoscopic procedure was performed under intravenous drug sedation using midazolam 3 mg and meperidine 30 mg with patient in left lateral decubitus position. The single endoscopist was blinded with the mode of bowel preparation regimen. Complete colonoscopy was considered when the colonoscope was passed from anus to cecum with good visualization of ileocecal valve and appendiceal orifice. Quality of bowel preparation was assessed and recorded by the endoscopist in the record form based on modified Aronchick scale (good, fair, and inadequate). The examination was performed during the withdrawal of colonoscope with withdrawal time of more than six minutes. All detected positive findings were characterized and recorded.

Outcomes

The primary outcome was side effect, tolerability, and compliance of bowel preparation. The secondary outcome was quality of bowel preparation.

Sample size and statistical analysis

Sample size calculation was based on poor quality of bowel preparation, which can occur at about 20%. With type I error = 5%, type II error = 20%, the calculated sample size was 76 patients.

Descriptive data were reported as percentage. Categorical variables were analyzed using Chi-square test or Wilcoxon rank test, as appropriate. A *p*-value smaller than 0.05 was considered statistically significant.

Results

Of the 80 patients who were eligible for the study, 42 patients were randomized in the 45 ml x2 doses of sodium phosphate group (Group A) and 38 patients were randomized in the 30 ml x3 doses of sodium phosphate group (Group B). Colonoscopy would not be performed in 11 patients due to their absence after randomization, four patients who did not have their record about quality of bowel preparation, and 35 patients who did not return their questionnaires. In group A, 35 patients were quality analyzed and 20 patients were tolerability analyzed. In group B, 30 patients were quality analyzed and 14 patients were tolerability analyzed (Fig. 1).

No significant difference of baseline characteristics between the two groups. The median age in group A was 59-year-old and in group B was 57-year-old ($p = 0.99$). Male/female ratio in group A was 21/21 and in group B was 20/18 ($p = 0.37$). The median weight was 63 kg in both groups. There was no difference in indication for colonoscopy in both groups with the two most common indications as suspected colorectal cancer and lower gastrointestinal bleeding (Table 1).

Regarding the quality of bowel preparation, there was no significant difference in quality of bowel preparation between two groups. Thirty-four patients

(97.1%) in group A and 29 patients (96.7%) in group B had good quality of bowel preparation. One patient had fair quality of bowel preparation in each group (Table 2).

In analysis about tolerability, no significant difference in nausea ($p = 0.73$), vomiting ($p = 1$), pain ($p = 0.25$), volume of feces per one times ($p = 0.20$), times of defecation ($p = 0.76$), times from last doses to last defecation ($p = 0.72$), and difficulty to eat ($p = 0.07$) (Table 3).

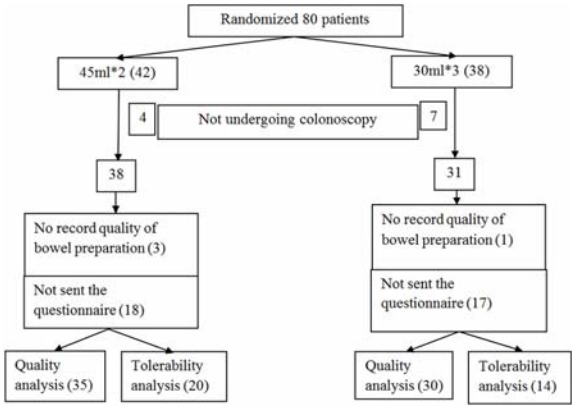

Fig. 1 Algorithm of randomization and analysis of our study.

Discussion

The goal of colonoscopy is to identify and remove all colorectal cancer-associated polyps. The visualization of the colonic mucosa together with a skillful colonoscopist are the keys for successful colonoscopy[1,2].

Oral sodium phosphate solution is a low volume, hyperosmotic solution that can induce osmotic diarrhea and result in colonic purgation[4]. The efficacy and tolerability of oral sodium phosphate solution as a colon cleansing solution prior to colonoscopy has been

Table 1. Baseline characteristics between 2 groups

Baseline characteristics	Group A 45 ml*2 doses (n = 42)	Group B 30 ml*3 doses (n = 38)	*p*-value
Age (years, median)	59	57	0.99
Sexes (male/female) (n)	21/21	20/18	0.37
Weight (kg, median)	63	63	0.82
Indication (n, %)			0.26
Screening	2 (4.8)	1 (2.6)	
Family history of colonic cancer	1 (2.4)	1 (2.6)	
Lower gastrointestinal bleeding	8 (19.0)	14 (36.8)	
Constipation	4 (9.5)	2 (5.2)	
Bowel habit change	6 (14.3)	1 (2.6)	
Colorectal cancer	13 (30.9)	14 (36.8)	
History of colonic polyp	7 (16.7)	3 (7.9)	
Abdominal pain	1 (2.4)	1 (2.6)	
Anemia	0	1 (2.6)	

Table 2. Quality analysis of both 2 mechanical bowel preparation regimens

Quality analysis of mechanical bowel preparation	Group A 45 ml*2 doses (n = 35)	Group B 30 ml*3 doses (n = 30)	*p*-value
Quality of bowel preparation			0.68
Good (n, %)	34 (97.1)	29 (96.7)	
Fair (n, %)	1 (2.9)	1 (3.3)	
Inadequate (n, %)	0	0	

Table 3. Analysis of tolerability between 2 groups of mechanical bowel preparation

Tolerability analysis mechanical bowel preparation	Group A 45 ml*2 doses (n = 20)	Group B 30 ml*3 doses (n = 14)	*p*-value
Nausea (n, %)	6 (30)	5 (35.7)	0.73
Vomiting (n, %)	2 (10)	2 (14.3)	1.00
Difficulty to eat	4 (20)	7 (50)	0.07

assessed in many studies[5-8]. In many clinical trials reported that oral sodium phosphate solution had significant better tolerability profile than PEG-based regimens with equal bowel cleansing[9,10].

Because of unpleasant taste or high volume, split dose of bowel cleansing agents or combination with other laxative agents has been reported to increase patient's acceptance and compliance[11,12]. Meta-analysis of the split-dose regimens has shown superior result to day-before bowel cleansing regimens and are preferred by patients[13].

Base on the concept of split dose of bowel cleansing regimen that may increase patient's acceptance and tolerability without decreasing its efficacy, our study compared the efficacy of two and three split doses of oral sodium phosphate solution. Only one prior study in 2004 by Barclay et al compared safety, efficacy, and patient tolerance of a three-dose regimen to conventional two-dose regimen. This prior study concluded that a three-dose regimen provides superior colonic cleansing without compromising volume status or serum biochemistry, but is associated with poorer overall patient tolerance compared with a conventional two dose regimens[14].

This prior study found that the 30 ml x3 doses provided equal efficacy in colonic cleansing, patient's tolerability, and acceptance compared to the 45 ml x2 doses of sodium phosphate solution. Nearly 97% of both groups had good bowel cleansing. A good compliance of mechanical bowel preparation regimens ingestion is a prerequisite for successful colonoscopy. Patients who can take more than 75% of the recommended amount of colonic cleansing agents are considered as good compliance[15]. Even 10% of group A and 14.3% of group B experience vomiting, both could complete their bowel cleansing regimens.

Our study was designed as a prospective, randomized, controlled trial. Numerous limitation factors were found such as small population, and some data loss from the questionnaires and medical records.

Conclusion

In summary, our study demonstrated that there is no difference in quality in mechanical bowel preparation and tolerability between the 45 ml x2 doses and the 30 ml x3 doses of sodium phosphate solution in patient undergoing colonoscopy.

What is already known on this topic?

Due to unpleasant taste or high volume, splitting of bowel cleansing agents has been reported to increase patient's acceptance and compliance. Regarding the efficacy of bowel cleansing regimens, previous reports of split-dose regimens revealed better quality of bowel preparation compared with single dose regimen.

Most of the previous reports were two split doses regimens.

What this study adds?

Our study demonstrated that splitting the bowel cleansing agent into three doses of sodium phosphate is a viable option for patient undergoing colonoscopy. It showed at least equal quality of bowel preparation and tolerability compared with the traditional two-split doses regimen.

Potential conflicts of interest

None.

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การศึกษาแบบทดลองสุ่มเปรียบเทียบการเตรียมลำไส้ใหญ่ก่อนการส่องกล้องด้วยสารละลายโซเดียมฟอสเฟตปริมาณ 45 ซีซี จำนวน 2 ครั้ง กับการใช้สารละลายโซเดียมฟอสเฟตปริมาณ 30 ซีซี จำนวน 3 ครั้ง ในผู้ป่วยที่มารับการส่องกล้องลำไส้ใหญ่

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ภูมิหลัง: การส่องกล้องลำไส้ใหญ่เป็นหัตถการที่จำเป็นในการวินิจฉัยและการรักษาโรคทางลำไส้ใหญ่และทวารหนัก การเตรียมลำไส้ใหญ่ให้สะอาดมีความสำคัญอย่างมากต่อการตรวจดูพยาธิสภาพของเยื่อบุลำไส้ใหญ่ สารละลายโซเดียมฟอสเฟตเป็นสารละลายที่ใช้เตรียมลำไส้ใหญ่ก่อนการส่องกล้องซึ่งมีผลข้างเคียงน้อยแต่ผู้ป่วยทนยาได้ไม่ดีนัก

วัตถุประสงค์: เพื่อเปรียบเทียบประสิทธิภาพและการทนต่อยาของการเตรียมลำไส้ใหญ่ในผู้ป่วยที่มารับการส่องกล้องลำไส้ใหญ่ ซึ่งถูกเตรียมลำไส้ใหญ่ด้วยสารละลายโซเดียมฟอสเฟตแบบ 45 ซีซี จำนวน 2 ครั้ง และการเตรียมแบบ 30 ซีซี จำนวน 3 ครั้ง

วัสดุและวิธีการ: ทำการศึกษาแบบทดลองสุ่มในโรงพยาบาลรามาธิบดี ระหว่างเดือนพฤศจิกายน พ.ศ. 2558 ถึงเดือนธันวาคม พ.ศ. 2559 เพื่อเปรียบเทียบประสิทธิภาพและการทนต่อยาของการเตรียมลำไส้ใหญ่ ผู้ป่วยจำนวน 80 รายที่มารับการส่องกล้องลำไส้ใหญ่ถูกแบ่งออกเป็น 2 กลุ่ม คือ กลุ่มศึกษา (เตรียมด้วยสารละลายโซเดียมฟอสเฟตแบบ 30 ซีซี จำนวน 3 ครั้ง) และกลุ่มควบคุม (เตรียมด้วยสารละลายโซเดียมฟอสเฟตแบบ 45 ซีซี จำนวน 2 ครั้ง) คุณภาพของการเตรียมลำไส้ใหญ่ถูกประเมินโดยผู้ส่องกล้อง และการทนต่อยาถูกประเมินโดยผู้ป่วยจากแบบสอบถาม

ผลการศึกษา: ผู้ป่วยจำนวน 80 ราย ที่ได้รับคัดเลือกเข้าร่วมงานวิจัยนี้ มีผู้ป่วยจำนวน 65 รายได้รับการวิเคราะห์เกี่ยวกับความสะอาดของการเตรียมลำไส้ และผู้ป่วยจำนวน 34 ราย ได้รับการวิเคราะห์เกี่ยวกับการทนต่อยา พบว่าไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติในเรื่องของลักษณะทั่วไปของผู้ป่วย ความสะอาดของการเตรียมลำไส้ ($p = 0.68$) อาการคลื่นไส้ ($p = 0.73$) อาการอาเจียน ($p = 1.00$) อาการปวด ($p = 0.25$) ความยากลำบากในการรับประทานยา ($p = 0.07$) ปริมาณของอุจจาระ ($p = 0.20$) ระยะเวลาจากยาครั้งสุดท้ายจนถึงการถ่ายอุจจาระครั้งสุดท้าย ($p = 0.72$) และความถี่ของการถ่ายอุจจาระ ($p = 0.76$) ระหว่างสูตรการเตรียมลำไส้ใหญ่ทั้ง 2 สูตร

สรุป: จากข้อมูลของการศึกษานี้พบว่าไม่มีความแตกต่างกันในคุณภาพของการเตรียมลำไส้ใหญ่ และการทนต่อยาระหว่างการใช้ยาเตรียมลำไส้ด้วยสารละลายโซเดียมฟอสเฟตแบบ 45 ซีซี จำนวน 2 ครั้ง และแบบ 30 ซีซี จำนวน 3 ครั้งในผู้ป่วยที่มารับการส่องกล้องลำไส้ใหญ่