

The First Clinical Experience with the Use of the Tablet Form of Sodium Phosphate Colokit in Preparation for Colonoscopy in Russia

PL Scherbakov^{1*}, TN Kalachnyuk², OI Ivanova², AA Arkhipov², RI Matorin² and M Yu Shcherbakova³

¹JSC 'Group of Companies' 'MEDSI', Russia

²Federal Scientific Clinical Centre of Physical - Chemical Medicine FMBA Russia, Russia

³RUDN University, Russia

*Corresponding Author: PL Scherbakov, JSC 'Group of Companies' 'MEDSI', Russia.

Received: May 13, 2020; Published: July 30, 2020

Abstract

Objective: To study various methods of preparing the intestines for instrumental studies, to evaluate the effectiveness and safety of sodium phosphates NaP (Colokit) for cleaning the colon in clinical practice.

Patients and Methods: We observed 63 patients and of these, 32 took the tablet form of NaP (Colokit). The control group consisted of 31 patients who were preparing for colonoscopy by the standard method using a two-mode preparation scheme with polyethylene glycol 4000.

Results: Adequate use of the tablet form of NaP was observed in 84% of patients. Compliance with using tableted forms NaP (Colokit) was as high, especially among patients, to which matured earlier uses in all other drugs for bowel preparation.

Conclusion: The use of Colokit (tablet form of NaP) in preparing the intestines for colonoscopy when compared with other cleaning methods showed good results both in the quality of preparation of patients and in the continuity of patients for this drug in preparation, as well as in the safety of its use, which is the same with data from other randomized trials.

Keywords: Sodium Phosphate Colokit; Colonoscopy

Introduction

Currently, colonoscopy is the most informative method for examining the condition of the mucous membrane of the colon. The greatest value of colonoscopy and is the ability to visualize in the early stages of formation of various neoplasms of the colon. That is why colonoscopy is widely used for screening studies in the detection of cancer of the digestive system [1,2]. Unfortunately, many patients currently have a negative attitude to the idea of them as a colonoscopy screening measures, particularly in the absence of any complaints on the part of the digestive system in general, and in particular of the intestine. However, the success of colonoscopy largely depends on adequate bowel preparation [4,5]. Unsuccessful primary preparation leads to an increase in the patient's negative attitude to the procedure, the need for repeated preparation, and an increase in the cost of colonoscopy [6].

Currently, there are three main groups of drugs used to prepare the intestines for instrumental research methods, including colonoscopy. These include: polyethylene glycols (PEG), and recently, along with traditional polyethylene glycols with a molecular weight of 4000,

new "low-volume" polyethylene glycols combined with an ascorbate complex with a molecular weight of 3,500 sodium phosphate and sodium picosulfate have appeared [7]. Previous experience of sodium phosphate in solution had dose that accurately serious problem, in particular, the risk of urinary system, electrolyte imbalance, the appearance of artifacts on the colonic mucosa, which sometimes significantly hampered performing differential diagnosis [1]. That is precisely why the use of drugs based on sodium phosphate solutions was limited by the recommendations of international pharmacological committees and commissions [8].

In recent years, there was a new tablet formulation of NaP (Colokit), safety and efficacy of which has been confirmed by many randomized clinical trials, which were compared with other drugs [7-11]. At the same time, according to many international researchers (Colokit appeared on the US pharmaceuticals market in 2006 and in the European market (France in 2010) [12] its application turned out to be more effective compared to the standard regimen of training 4 liters of polyethylene glycol. In addition, these same studies showed the complete safety of the use of the tablet form of sodium phosphate, in contrast to its liquid counterparts [12,13].

We also conducted a study of the effectiveness of intestinal preparation using a tablet form of NaP, compared to other modern means, according to the opinions of both patients and the doctors, who performed the colonoscopy, with a study of the consistency of drug administration, the quality of patient preparation and the safety of its use by other organs and systems.

Methodology

Study design

The study on the effectiveness of using Colokit for bowel preparation was observational, randomized, partially blinded. The main group consisted of 32 people who took Colokit. The control group consisted of 31 patients who used a standard two-component preparation scheme PEG - Fortrans - 2 + 2 liters to prepare for the study.

The study included male and female patients aged 18 to 65 years, for whom, according to various indications, a colonoscopy was prescribed. The division into groups was carried out by the method of simple randomization. The main group consisted of 32 people aged 18 to 65 years (mean age 42.6 ± 3.8 years). The control group consisted of 31 patients aged 18 to 65 years (mean age 43.5 ± 3.6 years). The exclusion criteria were contraindications and restrictions on the use of the drug Colokit indicated in the official instructions for the drug.

Bowel preparation and colon cleansing quality

All patients were advised to follow a low-fiber diet for 3 days before the start of the study.

In the main group of patients the bowel preparation regimen consisted of the oral acceptance of 32 tablets: the first part - the day before the study, ranging from 18 p.m. - 20 tablets (4 tablets every 15 minutes with 250 ml of any clear liquid), the second part - 12 tablets in the morning, every 15 minutes, 4 tablets, each serving with 250 ml of any clear liquid. On the day of the procedure - 4 - 5 hours before the examination, depending on the scheduled time of the colonoscopy.

Patients from the control group received Fortrans solution - 2 liters of solution, each of them for 1 hour, before the study and 2 liters of solution in the morning, on the day of the study, 4-5 hours before the procedure, depending on the time of the prescribed study. It was allowed to add acidifiers to the Fortrans solution in the form of lemon juice and an additional intake (at the request of the patient) of a clear liquid (in odes).

Subjective assessment of the quality of preparation of patients was carried out according to the questionnaire. The evaluation criteria were the following indicators: 1. Ease of taking the drug (easy, rather difficult, difficult), 2. Assessing the taste of the drug (no taste, almost no taste, unpleasant, but tolerable taste, intolerable to cous), 3. Presence of undesirable effects (nausea, vomiting, bloating, abdominal pain, irritation of the anus) 4. Desire to reuse the drug (yes, no).

Unbiased to quality bowel preparation was assessed by Boston Scales s bowel preparation (BBPS) [1,2,14,15]. The quality of bowel preparation was considered adequate if the BBPS score corresponded to 7 points or higher, since it is known that a score of 7 points makes it possible to detect polyps and neoplasms with a size of 6 mm or more in 88% of cases [16].

Statistical analysis was performed using the statistical software package Statistica 10.0, BioStat, MedCalc and Microsoft Excel. The Mann-Whitney test was used to compare the two groups of quantitative attributes; the χ^2 test and the Fisher exact test were used to compare the two groups of categorical attributes. In cases where the expected frequency for the investigated trait was less than 5, the methods of correlation analysis (Pearson and Spearman) were used. In an isolated comparison of the two groups, $p < 0.05$ was considered reliable.

Questionnaire data

All the doctors involved in the study, and the patients filled out special questionnaires.

The doctors recorded the following data for each patient: demographic data, presence of chronic diseases and the nature of the treatment, information about past surgeries, the results esophagogastroscopy, if it was performed, quality of cleansing the colon, colonoscopy results and adverse events.

The questionnaire, which was filled with independence of each the patient, about information on quantities in tablets taken in due course of administration; the quantity and nature of the fluid taken; and use of a diet low in fiber and its duration; side effects; willingness to use a similar training scheme repeatedly.

Monitoring of the further condition of the patients consisted of a telephone call 1 week after colonoscopy.

In the subgroup of patients who simultaneously with colonoscopy were esophagogastroduodenoscopy (24 and 16 respectively), was evaluated the state of the mucosa of upper parts digestive tract.

Results and Discussion

Characteristics of the patients

The most frequent concomitant chronic diseases were associated with the cardiovascular system (58.8%); disruption of endocrine systems or impaired metabolism and (15.8%), hypothyroidism (5.8%), diabetes (8.7%) and chronic gastrointestinal disease (7.5%) (Table 1).

Disease group	Main group (Colokit)	Control group (Fortrans)	Total
Hypertensive disease	9 (28%)	14 (45%)	23 (36.5%)
Heart rhythm disorders	8 (25%)	6 (19.4%)	14 (22.2%)
Metabolic syndrome	6 (18.8%)	4 (12.9%)	10 (15%)
Diabetes	4 (12.5%)	2 (6.4%)	6 (8.7%)
Hypothyroidism	1 (3.1%)	3 (9.7%)	4 (5.8%)
Chronic gastritis (including erosive)	14 (4) (43.8%/12.5%)	18 (6) (58.1%/19.4%)	32 (10) (51%/15%)
Gastric ulcer/duodenum	3/2 (9.3%/6.2%)	1/6 (3.2%/19.4%)	4/8 (6.3%/12.7%)

Table 1: Concomitant chronic diseases in the observed patients (abs. Numbers + %) (in groups).

56.7% of patients received at least one medicament, the most frequent of which were cardiovascular medicines (39.3%) and drugs for lowering cholesterol (26.9%).

As can be seen from the table, as a result of randomization, the distribution of patients according to gender and age composition and the nature of existing concomitant diseases in the main and control groups was almost the same ($p > 0.05$). Thus, all observed patients were on an equal footing in preparation for colonoscopy.

When carrying out the analysis of continuity (compliance) of taking the drugs, only one patient of the basic group during the pre-study there was an overwhelming sense Colokit inability to swallow the tablet, and the patient was excluded from the research. All other patients easily swallowed all 32 tablets at the recommended dosage. Moreover, 13 (40.6%) patients who had previously undergone colonoscopy noted an easier administration of the drug compared to the previous preparation with polyethylene glycol 2 + 2 liters - 7 people (21.9%) or low-volume polyethylene glycol 3,500 - 6 people (18.7%).

All patients taking Colokit noted that their urge to defecate began either immediately after taking the last portion of tablets (14 people - 43.8%), or within 15 minutes after the end of taking the drug. Most members of the main group were tested in the urge to defecate within 3 hours after ingestion, and emptying bowel occurred in 6-8 defecation acts. The first 3 - 4 urges took place with an interval of 15 - 20 minutes, further urges to defecate occurred with an interval of 30 - 60 minutes. During the night, patients felt and felt good, slept calmly, only 4 (12.5%) had rumbling in the abdomen and flatulence. In 3 patients of the main group (9.3%), there was a double urge to stool at night.

26 people of the first group (82%) easily drank all the necessary amount of liquid and 5 (15.6%) people experienced some difficulties drinking the last 2 servings of liquid.

29 people (91%) noted a complete or almost complete lack of taste in the drug, 2 patients (6.3%) did not like the taste of the drug.

When taking Colokit during preparation, 17 (53.1%) patients had various undesirable effects: most often - 7 people (21.9%) patients complained of nausea (feeling of heaviness in the stomach) when taking from 3 to 5 a portion of the liquid, in 6 people (18.7%) there was pronounced flatulence, rumbling in the abdomen, in 4 patients (12.5%) there were "wave-like" pains of a spastic nature along the intestine, with the passage of a peristaltic wave. 12 (37.5%) patients complained of itching, irritation of the anus. It should be noted, these undesirable events were observed only on the eve of the study. The morning dose all patients easily drank the proposed volume of the liquid. Any significant discomfort morning dose of the drug, none of the patients did not cause.

After taking the drug in the morning, the urge to defecate began 15-20 minutes after taking the last portion and continued for 40 - 90 minutes. The number of bowel movements did not exceed 5, with an interval of 15 - 20 minutes. 3 patients (9.4%) had a need for bowel movements when they arrived at the clinic. Moreover, the interval between the last bowel movement at home and the need to go to the toilet in the clinic was more than 1.5 hours. All patients easily moved from home to the clinic, which ranged from 40 minutes to 80 minutes, with 8 people (25%) using public transport. Of 32 patients of the main group, in 5 patients (15.6%), the time between the morning intake of the drug and the beginning of the prescribed study was 3 hours. However, the patients did not experience any discomfort and reached the separation from the house without manifesting urges to a chair. After a colonoscopy, 93.8% (30 people) expressed their willingness to take Colokit with repeated studies.

When comparing the profiles of patients who took PEG 2 + 2 L, we noted a more negative attitude to the use of this scheme.

All 31-patients who received PEG, took the entire volume of the designated fluid. Of the 31 patients in the control group, 10 (32.3%) patients used acidifiers (apple or lemon juice) when taking Fortrans. However, only 12 people (38.7%) took the entire volume of the drug with ease. 18 people (58%) noted that it was rather difficult for them to drink the entire volume of liquid, and 1 (3.2%) the patient noted that he drank the entire volume with great difficulty.

15 (48.4%) people at the reception like the evening and morning portion and with difficulties and complained of nausea. In three patients (9.7%), nausea was pronounced, with vomiting and in one patient (3.2%), vomiting was noted when taking an evening portion of the drug. Information about the difficult intake of 4 liters of PEG is confirmed by the results of studies of various authors. So, Kastenber, *et al.* reported vomiting in 18.5% of patients after taking the drug 4 L PEG [22].

Among patients of the control group, 18 (58.1%) people were previously trained for PEG colonoscopy. Only 4 members of this group (12.9%) noted that Fortrans had a neutral taste, the remaining patients noted that the taste of the solution was unpleasant 21 (67.7%) and even nasty - 6 people (19.4%) were too sugary or sugary -salty.

When taking Fortrans, the urge to defecate began 30 - 40 minutes after the start of taking the drug and lasted quite a long time for 4 - 5 hours. The interval between bowel movements was at the beginning of the process - 15 - 30 minutes, then 1 time in 40 - 80 minutes. 9 people (29%) complained of 3 - 4 times the urge to defecate during the night. After taking the morning portion of the drug, 14 people (45.2%) complained of nausea.

Flatulence when taking Fortrans bothered 23 patients (74.2%). Spastic abdominal pain along the intestines, while taking an evening portion, 18 people (58.1%) noted, and in the morning - 8 people (25.8%). Complaints of anus irritation were presented by 9 people in the control group (29%).

After morning reception, the urge to defecate ended in 28 persons (90.3%) within 2 hours, 3 patients (9.7%) for 3 hours. However, 6 patients (19.4%) needed to use the toilet upon arrival at the ward, immediately before the colonoscopy.

Willingness to be reused when preparing Fortrans to colonoscopy will be present, if each of, or low volume means tableted preparation expressed only 6 patients in the control group (19.4%).

During a telephone survey a week after the colonoscopy, none of the either patients in the main or control groups complained of their condition, somehow related to the procedure for preparing for a colonoscopy.

Criteria for evaluation		Colokit	Fortrans
Reception	Easy	26 (82%)	12 (38.7%)
	Pretty hard	5 (15.6%)	18 (58.1%)
	Hard	-	1 (3.2%)
Taste	Tasteless	29 (91%)	-
	Almost no taste	-	4 (12.9%)
	Unpleasant	2 (6.3%)	21 (67.7%)
	Nasty	-	6 (19.4%)
Nausea		7 (21.9%)	15 (48.4%)
Vomiting		-	1 (3.2%)
Bloating, flatulence		6 (18.7%)	23 (74.2%)
Abdominal pain		4 (12.5%)	18 (58.1%)
Anus irritation		12 (37.5%)	9 (29%)
Desire for reuse		30 (93.8%)	6 (19.4%)

Table 2: Comparative characteristics of subjective sensations of patients with various training schemes.

Thus, evaluating the subjective opinions of patients on the basis of the questionnaire, it can be reliably said that the use of Colokit is more preferable in comparison with traditional PEGs; when it is taken, significantly less adverse events are noted ($p < 0.05$).

The quality of colon cleansing was evaluated by endoscopists during colonoscopy. For endoscopists, this study was blinded, and the operators did not know in advance how the patients prepared.

Assessment of the quality of bowel preparation was carried out in accordance with the Boston scale of cleaning (BBPS) [1,2]. A good cleaning was considered to have ≥ 2 score for each segment of the colon.

When comparing the quality of treatment in the groups studied patients by endoscopists noticeable difference is not determined. So, in the main group, with Colokit preparation, good and excellent preparation was noted in 26 people (81.3%) with a quality of preparation of 9 points (3-3-3), in 3 (9.3%) - 8 points (3-3-2) and in 2 patients (6.2%) the total quality of preparation was estimated as 7 points (3-2-2). When assessing the quality of preparation using PEG in 27 (87.1%), the quality was excellent (9 points), in 2 (6.5%) - 8 points and in 2 (6.5%) patients the quality of preparation was rated at 7 points ($p > 0.05$).

At about administered colonoscopy various pathological changes in the colon summarily were detected in 45 patients (71.4%). Of these, benign epithelial formations, polyps, adenomas (including dentate adenomas) in 24 people (38.15%), malignant neoplasms in 5 patients (7.9%), diverticula in 36 patients (57.1%).

Considering the possibility of the formation of aft-like changes on the mucous membrane when using sodium phosphate described by other researchers [13] and having our own experience when using liquid forms of NaP [1,3], we paid special attention to the detection of such artifacts in patients taking Colokit, however, not one patient found them.

26 (81.3%) patients of the main group, who took the drug Colokit with colonoscopy, conducted and esophagogastroduodenoscopy. Of these, 11 (34.3%) people were found to have various changes in the mucous membrane of upper digestive tract. So, erosive esophagitis was determined in 4 people, submucous neoplasm of the stomach - in 1, hemorrhagic gastritis and erosion in the antrum in 3 (while taking non - steroidal anti - inflammatory drugs), cicatricial changes in the stomach in 2 and in one patient (3,2%) - flat surface erosion in the antrum. When determining *Helicobacter pylori*, the test result was positive in 6 people. In 10 patients, prior to colonoscopy, there was a history of previously existing lesions of the upper parts of digestive tract. A patient with an erosive lesion of gastric mucosa did not show any complaints of discomfort or pain. This may indicate a probable, but not proven connection between the occurrence of mucosal damage and taking the tablet form of NaP, which coincides with the data of previous post-marketing studies in France [17].

Neither one of the surveyed patients the results of tests carried out before and after preparation for colonoscopy, we did not observe any significant deviations of electrolyte balance, or disorders of the urinary system.

Thus, our study showed good continuity for patients with a new tablet form of sodium phosphate Colokit used to prepare for colonoscopy. The use of the morning dose of Colokit is possible even 3 hours before the colonoscopy, which improves the quality of life of patients. In addition, the results of the study can recognize the safety of taking the tablet form of sodium phosphate, which, unlike oral solutions, does not cause any noticeable changes in the electrolyte balance or affects the functioning of the urinary system, which is also confirmed by large randomized studies [18]. Besides, we confirmed the data meta-analyses, as well as the results of other authors and recommendations of the European Endoscopic Society (ESGE) which indicate higher effectiveness and safety of using the tablet form of sodium phosphate Colokit - to prepare patients for colonoscopy compared to traditional PEG usage [6-8,10,15-20].

That is why the drug Colokit should be used as an effective and safe drug for a high-quality bowel preparation, given specified restrictions in the instructions for use, and guided by international clinical guidelines [16,22,23].

Conclusion

The use of the tablet form of NaP Colokit in preparing the colon for colonoscopy when compared with other methods of purification showed good results both in the quality of the patient's preparation and in the continuity of the patients with this preparation in preparation and in the safety of its use, which coincides with the data of other randomized researches.

Bibliography

1. Shcherbakov PL and Knyazev MV. "Good bowel preparation is the key to highly informative colonoscopy results". *Effective Pharmacothera* PII 16 (2016): 14-20.
2. Shcherbakov PL., *et al.* "New bowel preparation for colonoscopy". *Attending Doctor* 11 (2014): 75-80.
3. Shcherbakov PL., *et al.* "Comparison of various schemes for preparing the intestines for instrumental research methods". *Doctor* 1 (2016): 59-64.
4. Froehlich F, *et al.* "Impact of colonic cleansing on quality and diagnostic yield of colonoscopy: the European Panel of Appropriateness of Gastrointestinal Endoscopy European multicenter study". *Gastrointestinal Endoscopy* 61.3 (2005): 378-384.
5. Harewood GC., *et al.* "Impact of colonoscopy preparation quality on detection of suspected colonic neoplasia". *Gastrointestinal Endoscopy* 58.1 (2003): 76-79.
6. Rex DK., *et al.* "Impact of bowel preparation on efficiency and cost of colonoscopy". *American Journal of Gastroenterology* 97.7 (2002): 1696-1700.
7. Tan JJ and Tjandra JJ. "Which is the optimal bowel preparation for colonoscopy- a meta-analysis". *Colorectal Disease* 8.4 (2006): 247-258.
8. Johanson JF, *et al.* "A randomized, multicenter study comparing the safety and efficacy of sodium phosphate tablets with 2L polyethylene glycol solution plus bisacodyl tablets for colon cleansing". *American Journal of Gastroenterology* 102.10 (2007): 2238-2246.
9. Lichtenstein GR., *et al.* "Clinical trial: sodium phosphate tablets are preferred and better tolerated by patients compared to polyethylene glycol solution plus bisacodyl tablets for bowel preparation". *Alimentary Pharmacology and Therapeutics* 26.10 (2007): 1361-1370.
10. Wruble L., *et al.* "Residue-free sodium phosphate tablets (OsmoPrep) versus Visicol for colon cleansing: a randomized, investigator-blinded trial". *Gastrointestinal Endoscopy* 65.4 (2007): 660-670.
11. Juluri R., *et al.* "Polyethylene glycol vs. sodium phosphate for bowel preparation: a treatment arm meta-analysis of randomized controlled trials". *BMC Gastroenterology* 11 (2011): 38.
12. Hagège H., *et al.* "Real-life conditions of use of sodium phosphate tablets for colon cleansing before colonoscopy". *Endoscopy International Open* 3.4 (2015): E346-E353.
13. Hassan C., *et al.* "Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) guideline". *Endoscopy* 45 (2013): 142-150.
14. Lai EJ., *et al.* "The Boston bowel preparation scale: a valid and reliable instrument for colonoscopy-oriented research". *Gastrointestinal Endoscopy* 69.3 (2009): 620-625.

15. Calderwood AH and Jacobson BC. "Comprehensive validation of the Boston Bowel Preparation Scale". *Gastrointestinal Endoscopy* 72.4 (2010): 686-692.
16. Heresbach D, et al. "[Consensus en endoscopie digestive: préparation colique pour la coloscopie totale chez l'adulte]". *Acta Endoscopica* 41 (2011): 39-46.
17. Belsey J, et al. "Systematic review: oral bowel preparation for colonoscopy". *Alimentary Pharmacology and Therapeutics* 25.4 (2007): 373-384.
18. Layton JB, et al. "Sodium phosphate does not increase risk for acute kidney injury after routine colonoscopy compared with polyethylene glycol". *Clinical Gastroenterology and Hepatology* 12.9 (2014): 1514-1521.
19. Heresbach D, et al. "Consensus in gastrointestinal endoscopy: preparation for full colonoscopy in 2011". *Acta Endoscopica* 41 (2011): 145-152.
20. Heresbach D. "What will 2013 bring in terms of bowel preparation before colonoscopy? Is form more important than substance?" *Acta Endoscopica* 43 (2013): 2-7.
21. Kastenberg D, et al. "Tolerability and patient acceptance of sodium phosphate tablets compared with 4-L PEG solution in colon cleansing: combined results of 2 identically designed, randomized, controlled, parallel group, multicenter phase 3 trials". *Journal of Clinical Gastroenterology* 41 (2007): 54-61.
22. Veselov V.V, et al. "Preparation of patients for endoscopic examination of the colon. Clinical recommendations". Moscow: Russian endoscopic something society (2011): 56.
23. VD Corleto, et al. "Efficacy of Prucalopride in bowel cleansing before colonoscopy: Results of a pilot study". *World Journal of Gastrointestinal Endoscopy* 9.11 (2017): 558-560.

Volume 7 Issue 8 August 2020

©All rights reserved by PL Scherbakov, et al.