

# BOWEL PREPARATION FOR PERFORMING A COLONOSCOPY: prospective randomized comparison study between a low-volume solution of polyethylene glycol and bisacodyl versus bisacodyl and a mannitol solution

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**ABSTRACT** – *Context* - Colonoscopy is currently the gold standard method to examine the colon, the rectum and the terminal ileum. In order to perform the colonoscopy, it is necessary to clean the bowel and use medications that are generally poorly tolerated by the patients. *Objective* - Compare the tolerability, acceptability, safety and efficacy of two solutions used for intestinal preparation for a colonoscopy. *Methods* - One hundred patients matched for sex and age were prospective randomized into two groups. Polyethylene glycol group received bisacodyl 10 mg plus 1 L of polyethylene glycol the night before and 1 L on the day of the exam. Mannitol group received bisacodyl 20 mg the day before and 1 L of a 10% mannitol solution on the day of the exam. The diet was the same for both groups. Tolerability and acceptability were measured using previously validated questionnaires. In terms of safety, variations in vital signs before and after the preparation were recorded, in addition to any complications. The quality of the preparation was graded based on the Boston and Ottawa scales. *Results* - Ninety-six percent (96%) completed the study. As for tolerability, the mannitol preparation group exhibited a significantly higher frequency of nausea, vomiting, abdominal pain, and abdominal distension than polyethylene glycol group ( $P < 0.05$ ). Acceptability was significantly better in polyethylene glycol group. The polyethylene glycol solution has also previously been shown to be safer than mannitol. No difference was observed in the quality of the preparation between the two preparation methods. *Conclusions* - The following conclusions can be made: polyethylene glycol solution had higher tolerability, acceptability, and safety than the mannitol and should be used instead of mannitol. Both preparation solutions have similar efficacy.

**HEADINGS** – Colonoscopy. Polyethylene glycol. Bisacodyl. Mannitol.

## INTRODUCTION

Colonoscopies are currently considered to be the procedures of choice for the investigation of diseases of the large intestine and the ileum in adults and children<sup>(2)</sup>. This is largely due to their diagnostic precision and the possibility of performing therapeutic procedures when abnormalities are found.

Despite technological advances in colonoscopies, ideal intestinal preparation still represents one of the most difficult stages of the process. Inadequate preparation results in an increase in costs and risks. There is a need for repetition of the examination due to the possibility of not detecting lesions, thus increasing the risk of complications<sup>(10)</sup>. There are various methods available for the preparation of the colon, each having its advantages and disadvantages.

For colonoscopies to be considered effective, it is fundamental that all mucosa of the organ are visible from the anal margin up to the ileocecal valve. In England, few services have been shown to reach 90% cecal intubation, and one of the main causes cited for incomplete exams is inadequate preparation<sup>(14)</sup>. A similar study performed in France analyzing 7,205 colonoscopies demonstrated that the examination of the colon and the rectum was complete in 96% of the cases, with inadequate preparation responsible for 32.5% of the incomplete examinations<sup>(5)</sup>.

A retrospective study of 93,004 colonoscopies in the United States demonstrated that the detection index of small polyps, less than 9 mm, was significantly greater after better preparation of the colon<sup>(9)</sup>. Another multicenter observational study that was performed in Europe with the participation of 11

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countries and analyzed 5,832 patients concluded that the quality of the intestinal preparation was significantly associated with the detection of polyps of any size<sup>(7)</sup>.

It is currently acknowledged that the ideal preparation should combine the following qualities: safety, efficacy, usability, tolerability, and low cost.

## Background

This study is justified by the use of a mannitol solution to prepare the colon in the majority of colonoscopy services in Brazil, although this solution is not recommended by the American Society for Gastrointestinal Endoscopy due to reports of colon explosion and electrolyte disturbances<sup>(18)</sup>.

The primary aim was to analyze the tolerability, acceptability, safety and effectiveness of two different solutions for intestinal preparation for colonoscopies: PEG balanced with electrolytes and mannitol.

## METHODS

This was a longitudinal, prospective, controlled and randomized study involving individuals undergoing colonoscopies for various indications with outpatient preparation in the Hospital das Clínicas of the School of Medicine of the University of São Paulo, SP, Brazil, from June to December of 2008.

The sample was calculated by estimating an alpha error of 5% and confidence interval with statistical significance of 5%, considering the strict exclusion criteria.

One hundred patients were matched for sex and age at a 1:1 ratio and randomized to receive the mannitol and bisacodyl solution or the PEG and bisacodyl solution.

All information about the preparation was clearly provided to each patient, and the colonoscopists were blinded about the bowel preparation.

The current study was approved by the Scientific Ethics Committee of for Analysis of Research Projects (CAPPesq) of the Clinical Board of the Hospital das Clínicas of the University of São Paulo - School of Medicine (research protocol number n0864/08).

This study does not present any conflicts of interest.

## Inclusion criteria

Patients between 18 and 85 years of age who underwent a colonoscopy with outpatient preparation and who signed an informed consent form were included in the study.

## Exclusion criteria

Patients with adynamic ileus, subacute bowel obstruction, a previous colectomy or colostomy, grade II to grade IV heart failure as per the New York Heart Association (NYHA) criteria, uncontrolled or severe systemic arterial hypertension, decompensate liver disease, severe dehydration, hypersensitivity to PEG, pregnancy or suspicion of pregnancy, severe intestinal inflammatory disease, toxic megacolon, presence of intense abdominal pain of unknown origin, chronic kidney disease, or severe constipation (one evacuation within an

interval greater than 5 days) were excluded from the study.

## Diet

The patients were instructed to follow a standard diet without solid food the day before the procedure.

### Group I: balanced PEG (Muvinalx<sup>®</sup>) and bisacodyl

The preparation was divided into two stages. The day before the examination, two 5 mg tablets of bisacodyl were given to the patient at 2 PM along with 1 L of the PEG solution at 8 PM on the same day. On the day of the examination, another liter of the solution was ingested, beginning at 07:30 (one of 10 200 mL cups every 10 minutes). Each liter of the PEG solution contained the following composition: 105 g of 3,350 Kd macrogol, 1.42 g of sodium bicarbonate, 2.8 g of sodium chloride, 0.37 g of potassium chloride, and lemon flavor. The consumption of clear liquids and water was freely permitted during the preparation in quantities up to 500 mL.

### Group II: mannitol and bisacodyl

The preparation was performed into two stages. The day before the examination, four tablets of 5 mg bisacodyl were taken orally, with two tablets taken at 10 AM and two tablets taken at 4 PM. On the day of the examination, the patient ingested 1 L of a 10% mannitol solution, beginning at 07:30. The consumption of clear liquids or water was freely permitted during the preparation in a quantity of up to 500 mL.

The use of two bottles of dimethicone (15 mL each at 75 mg/mL) was also included in both preparations.

For cases of abdominal pain, the patients were instructed to use Butylscopolamine 10 mg (Buscopam<sup>®</sup>), taken orally.

## Evaluation methodology of the colon preparation

The patients underwent the colonoscopy when the exit of clear rectal effluents into a toilet was confirmed by the researcher. This criterion is based on the principle of obtaining the best intestinal preparation possible, to prevent cancellation of the exam.

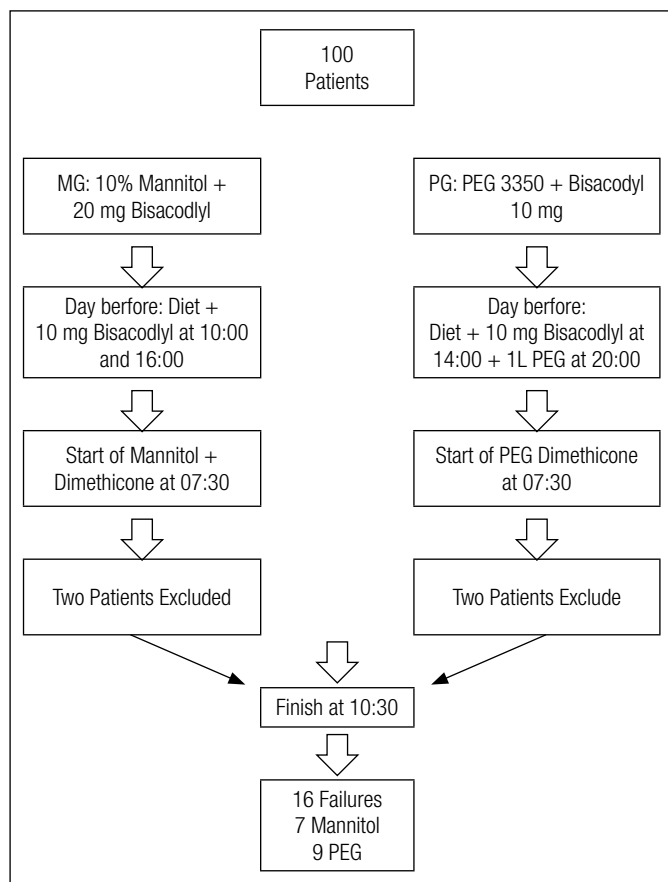
The team of colonoscopists scored the preparation according to the Ottawa and Boston preparation scales. The Ottawa scale verifies, in a simplified manner, the quality of the preparation of each segment individually and addresses the volume of liquid in an overall manner, generating a numeric result from 0 to 14<sup>(16)</sup>. The Boston scale assesses the quality of the preparation of each region separately on a scale of 0 to 3 for a total of up to 9<sup>(12)</sup>.

The preparation time was considered to last from the start of the ingestion of the solutions until the rectal effluent was clear and without fecal residue within a 3-hour time limit. The preparation was considered inadequate when the objective was not reached within this period. Inadequate preparations were complemented with additional doses of the solutions being evaluated.

A questionnaire to evaluate the tolerability of the preparation was administered by the researcher to all of the patients immediately before the colonoscopy. The intensity of the symptoms related to the preparation, such as nausea,

vomiting, abdominal pain, abdominal distension, and anal irritation, was evaluated on a scale from 0 to 5, classified for the best evaluation in three groups:

- 0 and 1: absent or light symptoms
- 2 and 3: moderate symptoms
- 4 and 5: severe symptoms



**FIGURE 1.** One hundred patients were matched for sex and age at a 1:1 ratio and randomized to receive the mannitol and bisocodyl solution or the PEG and bisacodyl solution as demonstrated above. Out of a total of 100 patients, 96 completed the study. When time finished, 16 patients were considerate failed and needed greater ingestion of medication to complete the preparation

The patients were also asked about the general acceptability of the preparation, evaluating the ease of medication ingestion (easy, moderate but tolerable, or very bad/not tolerable), the ease of liquid ingestion (easy, moderate, or difficult/very difficult) and whether they would accept the same type of preparation for a colonoscopy in the future.

With regard to safety, the patients were accompanied from the time they arrived at the hospital until their discharge, with variations in average blood pressure and heart rate evaluated before and after the preparation.

### Statistical methodology

In the descriptive analysis, the frequencies and percentages were calculated for the categorical variables, and the mean, standard deviation, median, minimum, and maximum were calculated for the continuous variables.

A chi-square test was used to compare the scale for age, sex, diverticular disease, and the identification of polyps according to the treatment medication. A Mann-Whitney test was used to compare the body mass index (BMI) and bowel habits, as well as the Boston scale, according to the type of preparation.

Chi-square and Fisher's exact tests were used to compare the following: side effects, the Ottawa and Boston scores, whether the patient would wish to use the same preparation in the future, the ease of ingesting the medication, the taste of the medication, and the ease of ingesting the liquid.

A significance level of 5% ( $P$  value  $\leq 0.05$ ) was used.

### RESULTS

Out of a total of 100 patients, 96 completed the study. Four were excluded for not having appropriately completed the preparation (Figure 1).

The groups were evaluated in relation to their distribution by age, BMI, sex, diverticular disease, bowel habits, and the frequency of polyps. Using a chi-square test ( $\chi^2$ ), it was concluded that the groups were homogenous.

No significant difference was observed when comparing the time used for adequate preparation between the tested solutions. When the index of failure was analyzed, 16 patients needed greater ingestion of medication to complete the preparation (Table 1).

**TABLE 1.** Comparisons between the mannitol solution and the PEG solution with regard to the preparation time and the failure index

Preparation time	Mannitol	PEG	Total	
Mean $\pm$ SD (min)	142.83 $\pm$ 61.26	144.67 $\pm$ 60.95	143.75 $\pm$ 60.79	0.8546**
Median (min)	141	119.5	128	
Minimum-Maximum (min)	50 - 340	60 - 320	50 - 340	
Total	48	48	96	
<b>Failure</b>				
No	41 (85.4%)	39 (81.3%)	80 (83.3%)	0.5839*
Yes	7 (14.6%)	9 (18.8%)	16 (16.7%)	
<b>Total</b>	<b>48</b>	<b>48</b>	<b>96</b>	

\*Chi-square test

\*\*Mann-Whitney test

A significant difference was observed in the occurrence of nausea, vomiting, abdominal pain, and abdominal distension according to the solution evaluated. The patients who used the mannitol solution had a greater intensity of nausea vomiting, abdominal pain and abdominal distension. No significant difference was observed in the occurrence of anal irritation (Table 2).

The analysis of acceptability revealed that the patients in the PEG group had a greater ease of ingesting the medication and the indicated quantity of liquid. They stated that the taste was more palatable in relation to the possibility of a future colonoscopy exam, and 96% would undergo the same preparation with balanced PEG vs 79% with mannitol group (Table 3). All of the results noted are statistically significant.

Analyzing the variation of the vital signs between the preparation methods, a significant difference was observed in relation to the heart rate both before and after preparation, according to the evaluated solution. No hemorrhagic

complication or colon perforation was reported, with a similar number of procedures being performed in both groups (Table 4).

No significant difference was observed between the scoring in the scales obtained for the evaluation of the quality of the preparation (Tables 5 and 6).

## DISCUSSION

Colonoscopy is considered to be the gold standard for the evaluation of the mucosa of the colon, rectum, and terminal ileum<sup>(17)</sup>. Therefore, a continuous search for perfection of the technique is merited for all stages of the colonoscopy.

For decades, the ingestion of PEG for intestinal preparation was considered to be the standard due to the low frequency of side effects. The PEG solution, however, requires the ingestion of large volumes, a characteristic that reduces the acceptability and tolerability of the patients<sup>(8)</sup>.

TABLE 2. Comparison between the mannitol and PEG solutions with regard to tolerability by patients

	Mannitol	PEG	Total	P-value
<b>Nausea</b>				
0 and 1	19 (39.6%)	32 (66.7%)	51 (53.1%)	0.0011**
2 and 3	19 (39.6%)	16 (33.3%)	35 (36.5%)	
4 and 5	10 (20.8%)	0 (0%)	10 (10.4%)	
Total	48	48	96	
<b>Vomiting</b>				
0 and 1	34 (70.8%)	43 (89.6%)	77 (80.2%)	0.0062*
2 and 3	6 (12.5%)	5 (10.4%)	11 (11.5%)	
4 and 5	8 (16.7%)	0 (0%)	8 (8.3%)	
Total	48	48	96	
<b>Abdominal pain</b>				
0 and 1	33 (68.8%)	29 (60.4%)	62 (64.6%)	0.0395*
2 and 3	11 (22.9%)	19 (39.6%)	30 (31.3%)	
4 and 5	4 (8.3%)	0 (0%)	4 (4.2%)	
Total	48	48	96	
<b>Abdominal distension</b>				
0 and 1	24 (50%)	30 (62.5%)	54 (56.3%)	0.0038**
2 and 3	14 (29.2%)	18 (37.5%)	32 (33.3%)	
4 and 5	10 (20.8%)	0 (0%)	10 (10.4%)	
Total	48	48	96	
<b>Anal irritation</b>				
0 and 1	26 (54.2%)	36 (75%)	62 (64.6%)	0.0612*
2 and 3	17 (35.4%)	11 (22.9%)	28 (29.2%)	
4 and 5	5 (10.4%)	1 (2.1%)	6 (6.3%)	
Total	48	48	96	

\*Fisher's exact test

\*\*Chi-square test

**TABLE 3.** Comparison between the mannitol and PEG solutions with regard to acceptability by patients

	Evaluated solutions		Total	P-value
	Mannitol	PEG		
<b>Ease of ingesting the medication</b>				
Easy	18 (37.5%)	36 (75%)	54 (56.3%)	0.0005**
Moderate	19 (39.6%)	10 (20.8%)	29 (30.2%)	
Difficult / very difficult	11 (22.9%)	2 (4.2%)	13 (13.5%)	
Total	48	48	96	
<b>Taste of the medication</b>				
No taste/light taste bad yet tolerable	31 (64.6%)	41 (85.4%)	72 (75%)	0.0184**
Very bad, not tolerable	17 (35.4%)	7 (14.6%)	24 (25%)	
Total	48	48	96	
<b>Ease of ingesting the liquid</b>				
Easy	17 (35.4%)	36 (75%)	53 (55.2%)	0.0002**
Moderate	19 (39.6%)	10 (20.8%)	29 (30.2%)	
Difficult/very difficult	12 (25%)	2 (4.2%)	14 (14.6%)	
Total	48	48	96	
<b>Would desire the same preparation in the future</b>				
No	10 (20.8%)	2 (4.2%)	12 (12.5%)	0.0136**
Yes	38 (79.2%)	46 (95.8%)	84 (87.5%)	
Total	48	48	96	

\*\*Chi-square test

**TABLE 4.** Comparison between the mannitol and PEG solutions with regard to patient safety

	Evaluated solutions		Total	P-value
	Mannitol	PEG		
<b>Increase in HR pre/post (bpm)</b>				
Mean ± SD	14.7 ± 8.93	8.79 ± 5.48	11.82 ± 7.94	0.0244***
Median	14	8	8	
Minimum - Maximum	2 - 40	3 - 20	2 - 40	
Total	20	19	39	
<b>Reduction in BP pre/post (mm HG)</b>				
Mean ± SD	3.83 ± 5.82	3.17 ± 6.14	3.5 ± 5.96	0.2361***
Median	0	0	0	
Minimum - Maximum	0 - 27	0 - 33	0 - 33	
Total	48	48	96	
<b>Procedure</b>				
Biopsies	2 (14.3%)	2 (11.1%)	4 (12.5%)	
Serial biopsies	2 (14.3%)	0 (0%)	2 (6.3%)	
Mucosectomy	1 (7.1%)	0 (0%)	1 (3.1%)	
Cold polypectomy	0 (0%)	2 (11.1%)	2 (6.3%)	
Polypectomy with forceps	3 (21.4%)	11 (61%)	13 (40.6%)	
Polypectomy/snare polypectomy	6 (42.9%)	3 (16.7%)	9 (28.1%)	
Total	48	48	96	

\*\*\*Mann-Whitney test

TABLE 5. Ottawa Scale according to the evaluated medication

Ottawa Scale	Evaluated medication		Total
	Mannitol	PEG	
Mean ± SD	5.31 ± 1.96	5.23 ± 2.01	5.27 ± 1.98
Median	6	5	6
Minimum - Maximum	1 - 10	0 - 9	0 - 10
Total for all patients	48	48	96

Mann-Whitney test: *P*-value = 0.9433

TABLE 6. Boston Scale according to the evaluated medication

	Group		
	Mannitol	PEG	Total
<b>Boston</b>			
Mean ± SD	8.5 ± 0.97	8.54 ± 0.99	8.52 ± 0.97
Median	9	9	9
Minimum -Maximum	5 - 9	5 - 9	5 - 9
Total for all patients	48	48	96

Mann-Whitney test: *P*-value = 0.6900

Even though the mannitol solution has been banned in various countries because of reports of cases of colon explosion during the performance of polypectomies<sup>(3,4)</sup> it is still widely used in Brazil. The objective of this study was to evaluate the tolerability, acceptability, safety and effectiveness of the PEG solution balanced with electrolytes and mannitol for intestinal preparation for colonoscopies.

There are a few studies comparing the two solutions in different forms of administration. In a study performed by Habr-Gama et al.<sup>(8)</sup> in 1984, 148 patients were randomized to receive one of the solutions prior to colonoscopy. No significant difference was observed in relation to the efficacy or the side effects, such as nausea, vomiting, abdominal pain, abdominal distention, and fainting; however, the side effects were not graded. In a study performed by Beck et al.<sup>(1)</sup> in 1986, comparing the same solutions that have been described for pre-operative bowel preparation in 80 patients, both methods were observed to be safe and effective with a success index of 70% to 100%.

In the present study, the tolerability was evaluated by applying a graded scale of side effects. In a comparison between the solutions, a significant difference was observed in favor of the balanced PEG solution for the following items: nausea, vomiting, abdominal pain, and abdominal distension. A study performed by DiPalma et al.<sup>(6)</sup>, which evaluated 200 patients who were administered the balanced PEG with a protocol similar to that used in the present study, revealed similar results. Lichtenstein et al.<sup>(13)</sup> obtained a similar result when they evaluated the balanced PEG solution combined with 20 mg of bisacodyl with regard to acceptability, using a questionnaire similar to the one in the present study. In that study, 206 patients were evaluated in the PEG group.

It is known that any solution for colon preparation may cause adverse effects. The most frequent are the following: hydroelectric disturbances, abdominal discomfort, nausea,

and vomiting. In the present study, although the frequency of hydroelectric disturbances was not evaluated in the laboratory, the balanced PEG solution proved to be more tolerable as judged by the majority of questions that were evaluated, corroborating previous information that suggests that a balanced PEG solution should be the method of choice for patients with comorbidities, such as renal failure, liver failure, or ascites<sup>(11)</sup>, as it is a non-osmotic and electrolytically balanced solution that does not cause fluid exchange between membranes, resulting in a low frequency of systemic electrolyte disturbances; its mechanism of action is explained by the high molecular weight of the macrogol polymer, which leads the solution to be retained in the colon when it is administered, favoring cleanliness of the colon<sup>(1)</sup>.

In the evaluation of the safety of the preparation, simplified measurements were used that are available in any medical center, along with simple evaluations of variations in blood pressure and heart rate. The patients who used the mannitol solution obtained a higher variation in their heart rate in relation to pre- and post-preparation, which indicates a greater possibility of electrolyte disturbances or hypovolemia.

One of the most severe and feared complications, colon explosion during the colonoscopy, initially reported by Bigard et al.<sup>(3)</sup> in 1979, has been the topic of a recent systematic review<sup>(11)</sup>. The literature describes 20 documented cases from 1952 to 2006, with 9 occurring during endoscopic procedures. Of these 9, 4 occurred during the performance of a polypectomy, resulting in colon perforation in all cases. Of the 4 cases, 2 were prepared with PEG, 1 with a sodium phosphate enema, and 1 with a mannitol solution. The most frequently used solution overall was mannitol, described in 14 cases, with sorbitol used in 1 case. In all of the cases cited, the risk factor was the production of gases at explosive levels. In the current study, 6 polypectomies with electrocautery were performed in the mannitol group, and 3 were performed in the PEG group, without any complications.

Nunes et al.<sup>(15)</sup> when comparing the solutions, found results that conflict with the present study, observing greater efficacy in the polyethylene group, with an optimal cleanliness of 90% in comparison to 75% of the mannitol group. In this study, the satisfaction index was similar, although only 55 patients were evaluated.

It should be highlighted that, in the present study, the efficacy of the preparation was evaluated by objective criteria through the Ottawa and Boston scales, both of which are current and internationally validated, and no significant difference was observed between the two methods.

## FINAL CONSIDERATIONS

It should be highlighted that the preparation for the examination was partly performed in the hospital for the convenience and safety of the patients. The importance of the verification of the exit of clear rectal effluents by the responsible team should be stressed as a factor in success. This resulted in no suspensions of the examination due to inadequate preparation. Regardless of sample size, patients

were randomized according to inclusion and exclusion criteria clearly defined. Despite the use of a questionnaire that was not formally validated, it contains questions that are similar to those used in other studies.

The preparation of the colon is usually a difficult stage for patients, and it is not uncommon for a patient to report that the preparation is worse than the exam itself. Thus, the search for an ideal preparation solution remains a goal that has yet to be achieved.

## CONCLUSIONS

In this study, we found that colonic preparation was equally efficacious using either a PEG solution or a mannitol

solution. Preparation of the colon with a PEG solution led to a significant improvement in tolerability, acceptability, and safety compared to mannitol solution.

## CAPSULE SUMMARY

To perform a colonoscopy, it is necessary to use solutions to clean the colon that are generally poorly tolerated by patients. The use of mannitol is still common in Brazil, although this use of mannitol for this purpose is banned in the rest of the world. In this study, we confirmed that the polyethylene glycol solution should be used on a large scale in a large country like Brazil because it is better accepted, well-tolerated and safer than the mannitol solution.

Vieira MC, Hashimoto CL, Carrilho FJ. Preparo de cólon para realização de colonoscopia: estudo prospectivo randomizado comparativo entre solução de polietilenoglicol baixo volume mais bisacodil versus solução de manitol mais bisacodil. *Arq Gastroenterol.* 2012;49(2):162-8.

**RESUMO – Contexto** - O exame de colonoscopia é atualmente o padrão-ouro para investigação do cólon e íleo terminal. Para sua realização há necessidade de limpeza do cólon com soluções que, em geral, são mal toleradas pelos pacientes. **Objetivo** - Comparar duas soluções de preparo intestinal para colonoscopia quanto à tolerabilidade, aceitabilidade, segurança e efetividade. **Métodos** - Cem pacientes pareados por sexo e idade foram randomizados prospectivamente em dois grupos. O grupo polietilenoglicol recebeu bisacodil 10 mg + 1 litro de polietilenoglicol na véspera e 1 litro no dia do exame. O grupo manitol recebeu bisacodil 20 mg na véspera e 1 litro de manitol 10% no dia do exame. A dieta foi a mesma nos dois grupos. A tolerabilidade e aceitabilidade foram aferidas por questionários previamente validados. Quanto à segurança foram avaliados: variação de sinais vitais antes e após o preparo e complicações, além de quaisquer sinais de complicação. A qualidade do preparo foi graduada através das escalas de Boston e Ottawa. **Resultados** - Noventa e seis pacientes (96%) completaram o estudo. Quanto à tolerabilidade o grupo manitol apresentou manifestação significativamente maior de náusea, vômito, dor abdominal e distensão abdominal do que o grupo polietilenoglicol ( $P < 0,05$ ). Aceitabilidade foi significativamente melhor com o grupo polietilenoglicol. O grupo polietilenoglicol também se mostrou mais seguro. Não se observou diferença na qualidade do preparo entre os métodos. **Conclusões** - A solução de polietilenoglicol apresentou melhor tolerabilidade, aceitabilidade e segurança e deve ser usada ao invés da solução de manitol. Ambas as soluções são semelhantes em eficácia.

**DESCRIPTORIOS** – Colonoscopia. Polietilenoglicóis. Bisacodil. Manitol.

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