



Original Article

Intestinal preparations for colonoscopy. Comparative study: mannitol, picosulphate and macrogol



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ARTICLE INFO

Article history:

Received 10 October 2017

Accepted 10 December 2017

Available online 3 February 2018

Keywords:

Colonoscopy

Bowel preparation

Mannitol

Sodium Picosulfate

Macrogol

ABSTRACT

Bowel preparation is mandatory prior to elective colonoscopy and their effectiveness is closely related to the quality of the examination. There are many preparations on the market and there is no consensus on which is best. This study aimed to compare three solutions for colon preparation in patients undergoing colonoscopy. We conducted a prospective study with 61 patients divided randomly into three groups: one that received a standard dose of macrogol, another received a standard dose of 10% mannitol and another received a standard dose of sodium picosulphate. Patients and examining endoscopists responded to questionnaires for compiling data. In the results we noticed that 10% mannitol, despite being less tolerated by the patient when compared to sodium picosulphate, presents better results in colonic cleaning, being therefore superior in this regard. Macrogol was considered as an intermediate in relation to the other two preparations. As for tolerability, preference is given to sodium picosulphate as best tolerated, followed by mannitol and by macrogol, which is poorly tolerated by the patient. We conclude that as the main objective of bowel preparation in colonoscopy is the quality of colonic cleaning, 10% mannitol was superior to the other preparations studied.

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Preparos intestinais para colonoscopia. Estudo comparativo: manitol, picossulfato e macrogol

R E S U M O

O preparo intestinal é mandatório antes da realização das colonoscopias eletivas e sua eficácia está intrinsecamente relacionada à qualidade do exame. Existem diversos preparos no mercado e não há consenso sobre qual é melhor. Este estudo teve como objetivo comparar

Palavras-chave:

Colonoscopia

Preparo intestinal

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<https://doi.org/10.1016/j.jcol.2017.12.001>

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Manitol
Picossulfato de sódio
Macrogol

três soluções para preparo de cólon em pacientes submetidos à colonoscopia. Foi realizado um estudo prospectivo com 61 pacientes distribuídos de forma randomizada em três grupos: um recebeu macrogol, outro manitol a 10% e outro picossulfato de sódio em doses padrão. Os pacientes e os endoscopistas examinadores responderam a questionários para compilação de dados. Nos resultados notamos que o manitol a 10%, apesar de ser menos tolerado pelo paciente quando comparado ao picossulfato de sódio, apresenta melhores resultados na limpeza colônica, sendo, portanto, superior neste quesito. O macrogol foi considerado como intermediário em relação aos outros dois preparos. Quanto à tolerabilidade, a preferência recai sobre o picossulfato de sódio como o mais bem tolerado, seguido pelo Manitol; macrogol foi o menos tolerado pelo paciente. Concluimos que, como o principal objetivo do preparo intestinal na colonoscopia é a qualidade da limpeza colônica, o manitol a 10% mostrou-se superior aos demais preparos estudados.

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Introduction

Colonoscopy is an increasingly used procedure because it allows direct visualization of the colonic mucosa. However, its effectiveness depends directly on a good bowel cleansing. The success of colonoscopy is linked to the efficacy of the colonic preparation.¹ This preparation consists of emptying the colon of all its fecal contents, thus allowing a complete verification of the mucosa. Therefore, it is considered the gold standard for the investigation of several disorders of the colon.²⁻⁴

Bowel preparation has also evolved a lot over time. At first, bowel cleansing lasted for several days.⁵ This cleaning strategy consisted of a special diet, repeated bowel washes, and the use of purgatives that caused many side effects, for example, severe intestinal cramps. In the 1970s, mannitol appeared, this was the first modification in the form of bowel preparation, a medication with a faster effect, better tolerated and with fewer side effects. Subsequently, other new drugs emerged, with varied actions and adverse effects.

The ideal preparation is one with superior efficacy, good safety, low monetary cost, ease of administration and excellent tolerance for the patient.⁶ However, despite the existence of several preparations in the market, there is not one that is currently considered perfect.

Regardless of the product used, this type of cleaning stimulates peristalsis and intestinal spasms, causing symptoms such as colic, abdominal distension, liquid diarrhea, hydro-electrolytic losses, and anal discomfort.¹

Currently, the most widely used methods for this purpose have been mannitol, macrogol or sodium picosulphate solutions.²

Mannitol (MANITOL, Fresenius Kabi, Itapeceira da Serra, Brazil) is one among several drugs available. This product has been used by parenteral route since the 1950s as an osmotic diuretic and renal vasodilator. However, it was only in the 1970s that mannitol was administered orally as a bowel preparation.

This preparation is digested by some bacteria, specifically *E. coli*.⁷ Because of its chemical characteristics and also because it is a polyol (sugar-alcohol), a nonabsorbable carbohydrate, when administered in high doses, causes osmotic diarrhea.⁵

Thus, mannitol was administered as a preparation of the large intestine for both surgeries and colonoscopic examinations.

When emerged as an alternative to colon preparation, mannitol was a great promise. It was expected that this would be a product with a rapid effect, easy administration, good patient acceptance, and few side effects. In addition, it was a cheap option.⁵ However, due to the dehydration that occurred after its use and the colonic blasts during electrocautery procedures, mannitol was abandoned in many countries. The United States is not adept at its use, because of the risk of colonic explosions, giving preference to macrogol solutions. In Brazil, Colombia, Cuba, and England, mannitol is widely used. As a consequence, new protocols of preparation began to be studied.⁸

Regarding dosage and administration, variations may occur among different Services. In general, 20% mannitol should be diluted in water in equal proportions and subsequently taken. The product can be ingested within 2 hours, which is known as “mannitol express”, or within 12 hours. However, when administered within 12 hours. This product should be administered in greater amounts.⁹ Mannitol can sometimes be diluted with lemon or orange juice, without bagasse, or in flavored water. This is done to improve the taste of the product because mannitol is very sweet, which can cause problems with its intake.^{2,8}

Generally, the result of the use of mannitol is described as favorable, for promoting an adequate cleaning in all segments. In addition, it is also considered as a fast cleaning method.⁹

Macrogol (MUVINLAX, Libbs Pharmaceuticals, Embu, Brazil) is a high-molecular-weight polyethylene glycol (PEG). When combined with electrolytes in an iso-osmolar solution for the purpose of bowel cleansing, this product is considered a good preparation for colonoscopy.^{1,5} This is a non-toxic solution, even when used in large quantities.¹ Macrogol associated with electrolytes is not absorbed by the colon and does not cause secretion of water and sodium, thereby reducing large fluid changes.

The great advantages of macrogol are to provide the same cleaning quality achieved by the other preparations used for colonoscopy, without limiting the risk of colonic explosion, since this preparation reduces the concentration of combustible intestinal gases to levels much lower than those

necessary for the occurrence of an explosion. This is one of the most relevant criteria for its choice, as well as its good tolerance and affordability.

Sodium picosulphate (PICOPREP, Ferring, São Paulo, Brazil) has also as active ingredients magnesium oxide and anhydrous citric acid.¹⁰

One of the most important characteristics of bowel preparations with sodium picosulphate is its ease of administration, both for its small volume and pleasant taste and for the tolerability reported by patients during its use.¹¹

Other types of preparations, for example, sodium phosphate (PHOSFO ENEMA, Cristália, Itapira, Brazil), magnesium (citrate or sulfate) salts, or lactulose (LACTULONA, Daiichi Sankyo, Barueri, Brazil), although still in use in some centers, are not among the products most used in modern endoscopic practice, and were not evaluated in this study.

The bowel preparation is intrinsically related to the morbidity of the colonoscopy exam.³ Adequate bowel cleansing is a directly associated factor to the correct diagnosis of the exam, lower chance of complications, lower cost, and lesser nuisance for the patient.¹

The ideal method of preparation should represent advantages in terms of efficacy, cost, safety, ease of administration, and patient tolerance.⁶ To this end, the method should meet a number of requirements, such as a short-duration laxative diet, a bearable volume, simple application, an efficient cleaning, absence of side effects, and low cost. However, a substance that has all these qualities together is not yet available.⁹

Since there is no ideal preparation for bowel cleansing, it is important to compare existing products, to suit their needs according to the needs of each patient. This motivated our group to study and compare the existing preparations in Brazil, and to evaluate which product would fit best in these characteristics.

Materials and methods

The present study was conducted as a prospective, randomized, unicentric, and no-control group study. The study was approved by the Research Ethics Committee (CEP) on July 29, 2015, through Opinion number 1,168,337. We began collecting the data on November 12, 2015, through the application of questionnaires; the collection ended on April 14, 2016.

The allocated patients came from two reference clinics in digestive endoscopy, both located in the city of Joaçaba, Santa Catarina. The prerequisites chosen for the selection of this group were 18 years of age or more, complete elementary education, and adequate clinical conditions for oral ingestion of the bowel preparation. The exclusion criteria were patients with an ileostomy, with suspected bowel obstruction, those severely ill, with an inability to oral intake, and who refused to participate in the study. Patients considered eligible received clarification on informed consent. These patients were able to freely decide whether or not to participate in the study. Patients who refused to participate received the preparation according to the routine protocol of the endoscopy service.

The procedures carried out were in accordance with the requirements of Resolution 466/12 of the National Health Council. Participants in the research were duly orientated

about the objectives of the study and with regard to their rights and safety, according to the Free and Informed Consent Form properly signed by each participant.

One of the inclusion criteria for participation in the study was to have a complete elementary course. The purpose of this criterion was basically that the patient had the capacity to respond to the questionnaire applied with minimal difficulty, both in reading and interpretation. This criterion was also established so that minimal bias could occur in the intake of the preparations since the correct use of solutions for bowel cleansing is fundamental for the quality of the exam.

We selected 61 patients who were randomly divided into three groups with the help of the Excel 2016 program (Microsoft®). Each group received one of three colonoscopy preparations. The preparations were delivered to the participants by the secretaries of the participating clinics, according to the randomization table, and the endoscopist did not know which of the three preparations would be used by each patient.

Bowel preparation started three days prior to the examination, with a restriction on some types of food, such as seeds, peanuts, nuts, fresh fruits, vegetables, salads, or multi-grain bread. On the day before the examination, patients were allowed only clear liquids and no solid food. On the day of the examination, two hours before its completion, an absolute fasting was ordered. These measures were followed according to the manufacturers' recommendations.

Of the 61 participants, 20 were allocated to the group that received 10% mannitol in a 1000 ml solution (500 ml of 20% mannitol diluted in 500 ml of filtered water). Filtered water was chosen instead of juices or flavored waters so that there was no masking of the real flavor of the solution. Another 20 patients were allocated to the macrogol group (16 sachets diluted in two liters of water). Finally, the remaining 21 subjects received sodium picosulphate (one sachet diluted in 150 ml of water, and then in 1.5–2 liters of water). In the three forms of colonic preparation, the regimens were performed twice the day before the examination.

On the day of the examination, the patients arrived at the center with the bowel preparation already done. Before the colonoscopy, the secretaries gave a questionnaire to the patients, consisting of four questions. These questions assessed the amount of water ingested, the quality of the taste, the interference in daily activities, and whether the patient would repeat the preparation again. After the test, another questionnaire was delivered to the endoscopist, who was unaware of the preparation that had previously been used by each patient. This questionnaire consisted of three questions: quality of the preparation, duration of colonoscopy until reaching the cecum, and if a complete examination was performed (with an evaluation of the terminal ileum).

The findings related to the quality of the preparation were evaluated in the questionnaire delivered to the endoscopists. These findings were recorded according to the Aronchick scale.¹ This scale is based on a visual estimate of the presence of fecal residues observed during the examination.

Statistical analysis was performed using BioEstat v. 5.0 program. For the comparison between data, the chi-squared test was applied, and we considered an alpha value ≤ 0.05 to reject the null hypothesis.

Results

The 61 cases studied were 36 (59.02%) men and 25 (40.98%) women, with a mean age of 52.76 years (19–80 years).

The quality of the colonic preparation in the group that used 10% mannitol was considered excellent in 17 patients (85.00%), good in 1 (5.00%), and fair in 2 (10.00%). For macrogol, 12 (57.14%), 7 (33.33%), and 2 (9.52%) patients considered the quality as excellent, good, and fair, respectively. In the group treated with sodium picosulphate, cleaning was considered excellent in 6 (30.00%) patients, good in 6 (30.00%) patients, fair in 7 (35.00%) patients, and poor in 1 (5.00%) patient. In no preparation, the cleaning quality was considered completely unsuitable. The difference was statistically significant ($p = 0.0064$) (Fig. 1).

It was also assessed whether or not the examiner completed the terminal ileum examination. In the group that received 10% mannitol, in 19 (95%) patients, the examiner completed the examination of the terminal ileum, and this was not possible in 1 (5.00%) patient. In patients receiving Macrogol, the terminal ileum was visualized in 15 (71.43%) cases, but in 6 (28.57%) cases, this did not occur. In the sodium picosulphate group, visualization occurred in 11 (55.00%) patients; in 9 (45.00%) cases, this was not possible. The difference was statistically significant ($p = 0.0123$) (Fig. 2).

The mean time taken to perform the colonoscopy in the 10% mannitol group was 18.63 minutes (SD = 7.32). For those who received macrogol, it was 22.12 minutes (SD = 8.4). Meanwhile, in the patients who received sodium picosulphate, the mean time was 23.06 minutes (SD = 7.9).

Concerning the interference caused by the preparations in normal activities in the life of the patients, the data found were: for the group that received 10% mannitol, 5 (25.00%) participants considered that the preparation interfered a lot, 4 (20.00%) that interfered little, 5 (25.00%) very little, and 6 (30.00%) considered that mannitol really did not interfere; in the PEG group, interference was, respectively, 2 (9.52%), 10 (47.62%), 3 (14.29%) and 6 (28.57%); and in the sodium picosulphate group, 2 (10.00%) patients considered that there was a lot of interference, 8 (40.00%) found that the preparation interfered little, 1 (5.00%) very little, and 9 (45.00%) that the preparation did not interfere at all. The difference was statistically significant ($p = 0.05$).

When asked if the participant would repeat the preparation on another occasion or if he would prefer to try another

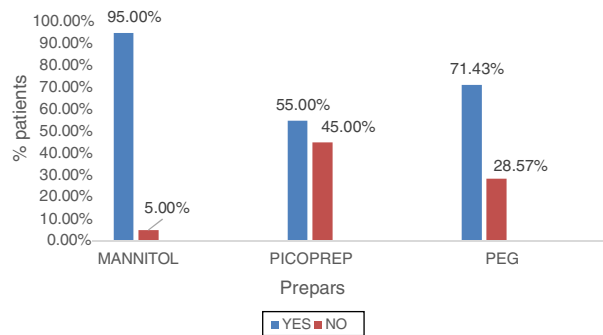


Fig. 2 – Number of complete examinations of the terminal ileum.

Source: The authors.

method, in the 10% mannitol group, 16 (80.00%) would repeat it and 4 (20.00%) would prefer to try another method. In those receiving macrogol, 16 (76.19%) would repeat it and 5 (23.81%) would prefer to change the preparation. Of the patients who received sodium picosulphate, 17 (85.00%) would repeat the preparation and 3 (15.00%) would prefer to change the preparation. There was no statistically significant difference ($p = 0.77$).

The taste of the preparation in the group that received 10% mannitol was considered excellent for 1 (5.00%) patient, good for 12 (60.00%), fair for 6 (30.00%), and bad for 1 (5.00%) patient. For the participants treated with macrogol, 1 (4.76%) considered the taste to be excellent, 8 (38.10%) considered it as good, 7 (33.33%) fair, and 5 (23.81%) bad. In the sodium picosulphate group, 1 (5.00%) patient considered the taste excellent, 14 (70.00%) considered it as good, 5 (25.00%) fair, and none of them considered the taste to be bad. The difference was not statistically significant ($p = 0.18$).

The amount of water ingested in the 10% mannitol group was considered bearable by 9 (45.00%) participants, relatively bearable by 8 (40.00%) patients, and poorly bearable by 3 (15.00%) patients. For those who received macrogol, the amount was bearable for 13 (61.90%) participants, relatively bearable for 2 (9.52%), and poorly bearable for 6 (28.57%). In the group receiving sodium picosulphate, the amount of water was considered to be bearable, relatively bearable, and poorly bearable for 16 (80.00%), 2 (10.00%), and 2 (10.00%) participants, respectively. The difference was considered statistically significant ($p = 0.03$).

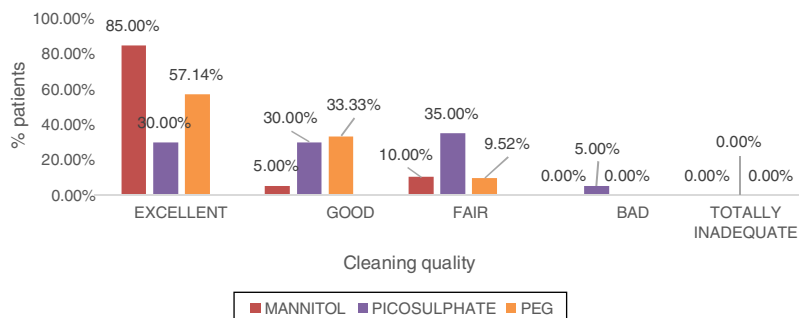


Fig. 1 – Quality of colonic cleaning.

Discussion

The preparation of the colon for colonoscopy is an essential procedure for a good visualization of the mucosa and a good quality of the examination. The critical purpose of this preparation is for obtaining a more accurate bowel cleansing, since an inadequately prepared colon may cause the examiner to pass unnoticed lesions that are concealed by debris. In addition, it is essential that the patient suffer the least possible discomfort in the ingestion of the preparation.^{1–4,12}

In this study, the quality of colonic cleaning had significant statistical significance, when comparing the three preparations studied. Of the patients who used mannitol, 85.00% obtained an excellent bowel cleansing; in only 10.00%, cleaning was considered fair. This data agrees with the literature on mannitol, macrogol and sodium picosulphate, evidencing that the quality of the preparation was considered better in patients who used mannitol.^{2,13–15}

However, some studies are in disagreement with the conclusions of the present study; one of them is that conducted by Forero in Colombia,¹⁰ that showed similarity in the quality of the colonic cleaning in relation to preparations with mannitol and with macrogol. In addition, another study conducted at the Universidade Federal de Alagoas hospital with 55 patients submitted to colonoscopy showed a better colonic cleaning in participants who used macrogol versus mannitol.¹⁶

Other drugs such as lactulose, even when associated with bisacodyl, present inferior results, being considered regular in 16.5% and poor in 4.3%, according to a study conducted in the Santa Casa de São Paulo. The present study allows us to conclude that there is a difference in the efficacy of the three bowel preparations compared. 10% mannitol demonstrated superior bowel cleansing quality versus sodium picosulphate and macrogol. Still, in regards to bowel cleansing, it was shown that macrogol was superior versus sodium picosulphate, the latter being the preparation with the worst result for cleansing. Our study also showed that, when comparing the tolerability of patients to the preparations studied, sodium picosulphate was better versus 10% mannitol and macrogol, thanks to the small volume ingested and the most palatable taste of that solution. As the main objective of a bowel preparation in colonoscopy is the quality of the colonic cleansing, we can infer that 10% mannitol was superior to the other preparations in the present study; thus, in our point of view this is the preparation of choice.¹⁷

Patients' acceptance should always be taken into account.² The discomfort caused at the time of bowel cleansing causes many patients to stop using the solution, or to misuse it. Therefore, the examination becomes inadequate, due to an improper use of the preparation.

Regarding the patient's acceptance of the solution, Miki Junior found a clear superiority of sodium picosulphate when evaluating the tolerance of intestinal preparations.¹³ This result was attributed to the combination of pleasant taste and the small volume of liquid that should be ingested with this product. These data confirm the results achieved in our study. In addition, the majority of patients using sodium picosulphate reported no interference with their normal daily activities.

Still, in relation to the amount of water ingested, macrogol was the preparation with a higher percentage of patients who considered as bad the amount of liquid for intestinal preparation. Only 61.90% of those using macrogol reported that the amount of water ingested was bearable. This data was statistically significant ($p=0.03$) and reinforces the percentage of 23.81% relative to those patients who stated that they would not repeat macrogol and would try another method. The literature agrees with our study because it highlights the patients' poor acceptance of this substance – which is why macrogol has been substituted by other solutions, according to the study by Santos Junior conducted in the countryside of the state of São Paulo.⁵

The analysis of interference with normal activities of the patients using the preparations studied revealed statistical significance ($p=0.05$). Although mannitol causes greater abdominal distension versus sodium picosulphate and, consequently, a greater discomfort with its use, these two methods of preparation were well accepted by the patients, according to Muller et al.¹⁸ This fact disagrees with our findings, which demonstrated, with statistical evidence, that among the three preparations compared, sodium picosulphate is the best-tolerated product.

Regarding the possibility of reusing the same bowel preparation again, most of the users of sodium picosulphate responded that they would use the product again. Consequently, most patients using sodium picosulphate reported no interference with their daily tasks.

This data interconnection was not observed in our mannitol analysis, because although being considered as the preparation that most interfered with the normal activities of the patient, most of the interviewees in the present study answered that they would have no problem in using mannitol again.²

Conclusion

The present study allows us to conclude that there is a difference in the efficacy of the three bowel preparations compared. 10% mannitol demonstrated superior bowel cleansing quality versus sodium and macrogol picosulphate. Still, in regards to bowel cleansing, it was shown that macrogol was superior versus sodium picosulphate, the latter being the preparation with the worst result for cleaning. Our study also showed that, when comparing the tolerability of patients to the preparations studied, sodium picosulphate was better versus 10% mannitol and macrogol, thanks to the small volume ingested and the most palatable taste of that solution.

As the main objective of a bowel preparation in colonoscopy is the quality of the colonic cleaning, we can infer that 10% mannitol was superior to the other preparations in the present study; thus, in our point of view, this is the preparation of choice.

Conflicts of interest

The authors declare no conflicts of interest.

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