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Quality of bowel preparation and adenoma detection: does fractionated dosing make a difference?

Qualidade do preparo intestinal e detecção de adenomas: a dose fracionada faz diferença?

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ABSTRACT

Introduction: Colorectal cancer is responsible for at least 880,000 deaths annually worldwide. Colonoscopy is the gold standard in screening for this cancer, and adequate colonic preparation is essential.

Objective: To evaluate the quality of colonoscopic preparation using the Adenoma Detection Rate (ADR) and Boston Biopsy Score (BBPS), according to the preparation proposed to participants.

Method: Two groups were included. The first, with 32 participants, received a divided dose of sulfate solution with one dose the day before the examination. The second, composed of 19 participants, received the same solution in a single dose only the day before the examination.

Result: ADR was higher in the first group. Participants who received a purgative the day before the examination had greater sleep disturbance. Both the cecal intubation rate and the rate of adequate and excellent examinations (BBPS) were higher in the group receiving the divided dose. There was no significant difference when comparing the tolerability of the preparation between the 2 groups.

Conclusion: Splitting the purgative dose proved effective, improving the cecal intubation rate and ADR.

KEYWORDS: Colorectal neoplasms. Intestinal polyps. Gastrointestinal endoscopy. Colonoscopy. Screening programs.

RESUMO

Introdução: Câncer colorretal é responsável por pelo menos 880.000 mortes por ano no mundo. A colonoscopia é o padrão ouro no rastreio desse câncer, e o preparo colônico adequado é fundamental.

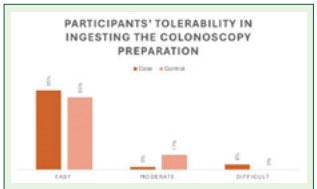
Objetivo: Avaliar a qualidade do preparo colonoscópico através da Taxa de Detecção de Adenoma (TDA) e Escala de Boston (BBPS) conforme o preparo proposto aos participantes.

Método: Foram incluídos 2 grupos. O primeiro, com 32 participantes, recebeu dose dividida de solução de sulfato com 1 dose da solução às vésperas do exame. O segundo, composto por 19 participantes, recebeu a mesma solução em dose única apenas no dia anterior ao exame.

Resultado: TDA foi maior no primeiro grupo comparativamente. Os participantes que receberam purgativo às vésperas do exame apresentaram maior distúrbio de sono. Tanto a taxa de intubação cecal quanto a de exames adequados e excelentes (BBPS) foram maiores no grupo que recebeu a dose dividida. Não houve diferença significativa quando se estudou a tolerabilidade em realizar o preparo comparando ambos os grupos.

Conclusão: dividir a dose do purgativo mostrou-se efetiva, melhorando a taxa de intubação cecal e a TDA.

PALAVRAS-CHAVE: Neoplasias colorretais. Pólipos intestinais. Endoscopia gastrointestinal. Colonoscopia. Programas de rastreamento.



Tolerance in ingesting bowel preparation

Central Message

Adenoma detection rate is a quality indicator in colorectal cancer screening. A task force by American Society for Gastrointestinal Endoscopy determined that a colonoscopy service should be capable of detecting polyps in at least 25% of patients undergoing colorectal cancer screening, with 30% for men and 20% for women. Achieving a high adenoma detection rate is strongly associated with favorable clinical outcomes.

Perspective

In the present study, the adenoma detection rate was higher among participants who received a split-dose regimen, with the second dose administered on the morning of the procedure, compared to those who received the purgative only on the day before

Supplementary Material - Instructions for split-dose colonoscopy preparation

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INTRODUCTION

In 2022, 20,245 people died from colorectal cancer (CRC) worldwide. There were approximately 45,000 new cases. It´s incidence varies depending on the region of the world, being more common in Australia, New Zealand, Europe, and North America, while the lowest are seen in Africa and Central and South Asia.[1]

Globally, according to one study conducted in 2018, approximately 880,000 people died from CRC.[2] It was observed that both incidence and mortality vary according to the Human Development Index (HDI) of the countries. Nations undergoing rapid economic transition, such as Brazil, have shown an increase in both incidence and mortality rates. Countries with a high HDI had increased incidence and decreased mortality, while those with very high HDI experienced a reduction in both rates.[3]

It is well known that most CRCs arise from the adenoma-carcinoma sequence. Vast majority of adenomas appear as intestinal polyps, which are detectable through endoscopic imaging examinations. Thus, colonoscopy becomes a powerful tool in the early diagnosis of CRC.

It´s screening current recommendation in the general population is to begin at age 50, starting 5 years earlier in the African descendent population, according to the American Society for Gastrointestinal Endoscopy (ASGE).[4] Nevertheless, organizations such as the American Cancer Society recommend screening starting at age 45 for individuals at average risk, with screening beginning 5 years earlier for high-risk populations or 10 years before the age at which a first-degree relative was diagnosed.[5]

Both the Brazilian Society of Coloproctology and the National Cancer Institute (INCA) maintain the recommendation to begin screening for intestinal polyps at age 50 for individuals at intermediate risk. The interval between colonoscopies remains every 10 years if the risk is low.

Adenoma detection rate (ADR) is a quality indicator in CRC screening. A task force by ASGE determined that a colonoscopy service should be capable of detecting polyps in at least 25% of patients undergoing CRC screening, with 30% for men and 20% for women. Achieving a high ADR is strongly associated with favorable clinical outcomes.[4]

It is known that adenoma removal through screening can prevent CRC development, and early diagnosis of localized cancer reduces mortality.[6] Among the various screening strategies and tests, colonoscopy has high sensitivity and specificity and provides the benefit of removing lesions during the procedure.

Colonoscopy allows for visualization of the rectum, colon, and the distal portion of the terminal ileum. It is both a diagnostic and therapeutic procedure, considered the gold standard for CRC screening and surveillance. A successful colonoscopy requires adequate bowel preparation. Excellent bowel preparation is extremely important as it allows proper visualization of the entire colonic mucosa and enhances the safety of therapeutic maneuvers.

Thus, adequate colonoscopic preparation is necessary for optimal colonic visualization. Split-dose preparation using purgatives, with one dose the day before and another on the day of the procedure, has proven superior to single dose preparation the day before the exam. According to the task force, the second dose should be taken 3-8 h before the procedure. This practice has shown to increase the ADR and improve patient acceptance of the preparation.[4]

Currently, the colonoscopy service at the hospital in this study conducts bowel preparation only on the day before the procedure. A recent study carried out at this facility found that approximately 25% of colonoscopies had inadequate or partially adequate preparation, which sometimes resulted in incomplete exams. Thus, an increase in ADR is expected with the addition of a purgative dose on the eve of the colonoscopy.

According to ASGE recommendations, an optimal screening exam requires adequate preparation and cecal intubation with photographic documentation. Incomplete examinations increase the risk of interval cancer and reduce ADR.

The primary objective of this study was to determine the ADR and cecal intubation rate according to the type of bowel preparation administered to patients at the CRC screening outpatient clinic to establish a quality indicator. The secondary objective was to evaluate correlations between the 2 types of bowel preparation in relation to age, sex, race, tolerability of each preparation through a standardized questionnaire, and characterize the epidemiological profile of the detected polyps according to histological type, size, and the presence or absence of high-grade dysplasia. The main objective of this study was the potential improvement in the quality of CRC screening and reduction of interval cancers.

METHOD

Research project was submitted to the Research Ethics Committee of Evangelical Mackenzie Faculty of Paraná, Curitiba, PR, Brazil and approved. The study required the signing of an Informed Consent Form by each patient invited to participate.

This is a longitudinal and individualized experimental study (clinical trial), in which a total of 84 candidates were selected. Among these, 52 composed the "case" group, in which participants received 1 dose of purgative the day before and another on the morning of the colonoscopy procedure. The "control" group included 32 participants who received a single-dose laxative preparation only on the day before the colonoscopy. Of the case group participants, 46 accepted the procedure after being invited, and 32 effectively underwent colonoscopy on the scheduled date.

In the control group, out of the 32 selected participants, 19 effectively completed the preparation and underwent the procedure on the scheduled date. The remaining 4 withdrew, while the others awaited

scheduling in the hospital's endoscopy service. Data were collected from patients indicated for CRC screening who were admitted to the outpatient clinic of the Mackenzie Evangelical University Hospital, Curitiba, PR, Brazil. Inclusion criteria included: age over 50, or 40 if there was a family history of CRC; asymptomatic status; no previous diagnosis of CRC; and no prior colonoscopy. Symptomatic individuals (e.g., gastrointestinal bleeding, recent bowel habit changes, weight loss, pencil-thin stools, prior CRC history) and those not meeting extended age criteria were excluded. Participant recruitment for the case group occurred between June and August 2024. Control group recruitment took place from November to December 2024. Participants in each group were consecutively enrolled until the required number was achieved. There was no randomization in this study. According to prior authorization, it was provided a split-dose colonoscopy preparation protocol using a sulfate solution (sodium picosulfate, magnesium oxide, anhydrous citric acid – Picoprep®) to the case group, and a single-dose protocol the day before the procedure to the control group. All participants were educated about the proposed dietary restrictions, fluid intake volumes, and timing of the doses. Each subject was monitored up to the date of their procedure. A database in Excel was used to track basic demographic data and examination dates. On the day of the colonoscopy, a structured questionnaire was administered to assess tolerance to the preparation, adverse events, and other relevant symptoms (see Supplementary Material at article´s end).

In the case group, patients received 2 doses of Picoprep® at different times: one at 6:00 PM the day before and one around 5:00 AM on the day of the exam, according to ASGE recommendations. For the control group, participants ingested the first sachet at 6:00 PM and the second at 10:00 PM the day prior to the procedure. Fasting began at 10:00 PM the night before the colonoscopy for both groups (solid and semi-solid foods). Clear liquids were allowed up to 2 h before the exam. The proposed diet included lowfiber processed or mashed foods such as potatoes, sweet potatoes, cassava, yams, rice, and lean poultry or fish. Foods high in fiber, carbonated beverages, colored juices, and others that could hinder visualization during the procedure, were prohibited. Each patient was instructed on the importance of intestinal preparation, fluid intake, physical activity on the day before the procedure, and the need for a companion on the examination day.

The questionnaire was based on validated studies to assess adverse effects and preparation tolerability, including nausea, vomiting, sleep disturbances, falls, fainting, abdominal pain, bloating, and anal irritation. Age, sex, and race were also collected. Patient understanding and adherence to preparation instructions were evaluated.

Colonoscopy reports were analyzed based on the Boston Bowel Preparation Scale (BBPS) and the following criteria: completeness of the exam, presence/absence and number of polyps, size, location, and presence of lesions suggestive of neoplasia. A complete exam was defined as one that identified anatomical landmarks such as the ileocecal valve or terminal ileum. BBPS scores above 7 were considered adequate. Examinations were also rated based on the endoscopist's subjective impression (adequate or inadequate). Exams interrupted due to poor preparation or anatomical limitations were labeled as incomplete.

Polyps were classified by histologic type, location, size, and presence of high-grade dysplasia. The categories used were hyperplastic polyps, tubular adenomas without high-grade dysplasia, and tubulovillous adenomas without high-grade dysplasia. No other histologic types were identified in this cohort.

Sedation was performed mostly by the endoscopist, with anesthesiologists involved only in selected cases. Sedatives used included benzodiazepines, fentanyl citrate, or propofol.

Risks associated with the procedure and preparation included dehydration, falls, nausea/vomiting, abdominal discomfort, rectal pain, diarrhea, syncope, hypersensitivity, renal impairment, intestinal perforation, gastric ulcers, and paralytic ileus. However, no urgent medical events were observed.

Statistical analysis

Results were summarized using descriptive statistics for quantitative variables and contingency tables for categorical variables. Group comparisons were conducted using the Chi-square or Fisher's exact test (for small samples) for categorical variables, and the Mann–Whitney U test for continuous variables. Data analysis was performed using Statistica software, version 7.

RESULT

Among the participants in the group submitted to the split-dose bowel preparation, 47% were male and 53% were female. In contrast, among those who received the single-dose preparation, 37% were male and 63% female. There was no statistically significant difference between the groups regarding participants' sex (p=0.48).

Regarding age, the mean age of participants in the split-dose group was 60 years, with a minimum age of 41 and a maximum of 83 years. The control group had a lower mean age of 57 years, ranging from 50-67 years There was no statistically significant difference between the groups in terms of age (p0.31).

Upon analyzing the self-reported race of participants based on the questionnaire applied after the examination, the majority identified as "white," with a higher proportion observed in the split-dose group, where 91% of participants self-identified as white. In the control group, although to a lesser extent, 72% of participants also identified as white. Individuals identifying as mixed-race ("pardo") or black comprised a minority in both groups (Figure 1). There was no statistically significant difference between the groups regarding participants' race.

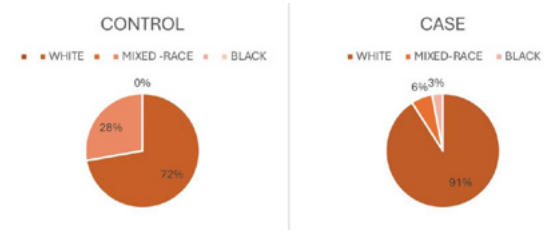

FIGURE 1 — Race of participants

When analyzing the quality of bowel preparation in the colonoscopies performed, the average BBPS score among patients was 6. A greater number of participants demonstrated inadequate preparation according to our criteria (BBPS <7). Among the participants who received a split-dose regimen, with 1 dose taken on the day of the examination, 20 participants (62.5%) presented with inadequate preparation (BBPS <7), while only 12 (37%) achieved a BBPS ≥7.

Among those who received a single dose of purgative the day before the examination, the results followed a similar trend observed in the case group: 61% presented with BBPS <7 and 39% met the criteria for adequate preparation. No statistically significant difference was found between the groups regarding BBPS scores (Figure 2, p=0.3).

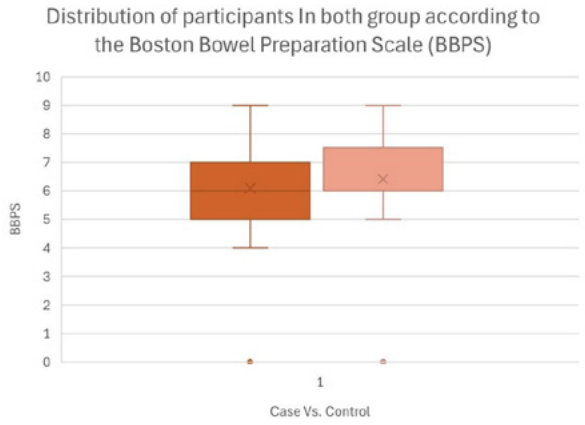

FIGURE 2 — Bowel preparation distribution in both groups according to BBPS scale

Regarding the cecal intubation rate (complete examinations with photographic documentation), both groups and demonstrated satisfactory results. Among participants who received a dose of purgative on the day of the examination, 94% underwent a complete examination. In the group that received the purgative only on the day prior to the procedure, 81% achieved a complete examination (Figure 3). There was no statistically significant difference between the groups in terms of cecal intubation rate (p=0.20).

Polyp detection rate was higher among participants who received a purgative dose on the day of the procedure: 31% of these individuals had polyps identified at the end of the examination, compared to 26% of participants who did not receive the split-dose regimen (p = 0.78). Regarding the size of the polyps found in both groups, it was observed that participants in the case group had a smaller mean polyp size compared to the control group, 5.88 mm vs. 8 mm, respectively (Figure 4, p=0.78).

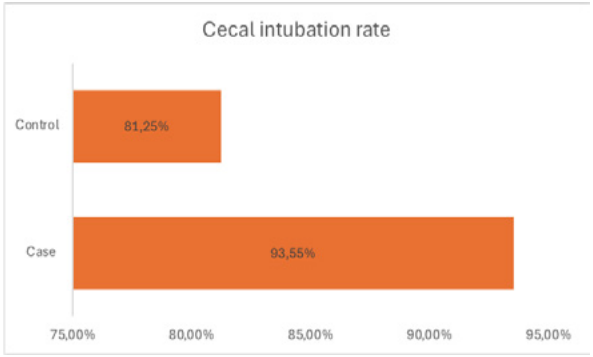

FIGURE 3 — Cecal intubation rate

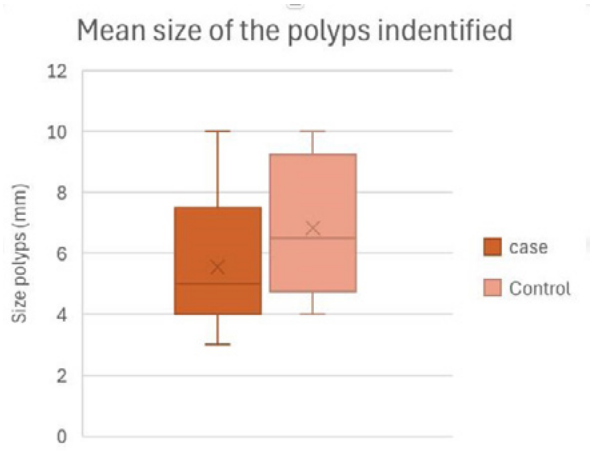

FIGURE 4 — Mean size of identified polyps

When analyzing the ADR, it was observed that participants who received a purgative dose on the day of the examination had a higher ADR compared to the control group: 22% of the polyps found in the case group were adenomas, vs. only 15.79% in the control group (Figure 5, p=0.36).

The histological types of adenomas identified after the examinations consisted of 3 types (Figures 5 and 6), none of which showed high-grade dysplasia, serrated histology, or adenoma size greater than 1 cm. Majority of participants in both the case and control groups had tubulovillous adenomas without dysplasia as the main histological finding. Other histological types identified were hyperplastic polyps and villous adenomas.

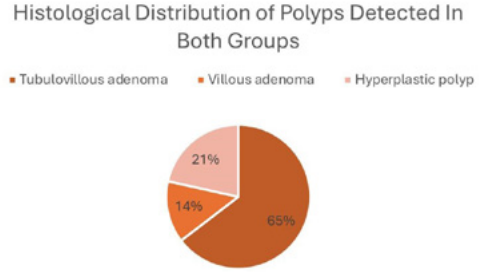

FIGURE 5 — Histological distribution of polyps

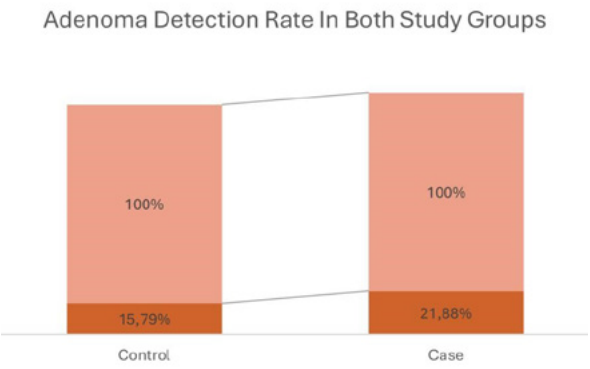

FIGURE 6 — Adenoma detection rate in both groups

The results of the questionnaires administered after the colonoscopy differed when comparing participants who received a purgative dose on the day of the examination vs. those who received it only on the previous day.

When participants were asked, "How difficult was it for you to ingest the studied medication?", 91% in the split-dose group reported ease of ingesting the laxative solution. The control group also reported ease of ingestion, with 83% indicating no difficulty. Only two participants in the case group found the ingestion of the solution difficult (Figure 7, p=0.65).

Among the analyzed symptoms, were considered nausea, abdominal pain, abdominal distension, anal irritation, sleep disturbance, falls and bruises, and syncope to assess the tolerability of the bowel preparation in each group. Sleep disturbance was reported by 47% of participants who received the purgative dose on the morning of the examination, with 26% reporting mild, 12% moderate, and 9% severe sleep disturbance. In contrast, when the same question was posed to the group that did not ingest the purgative during the night, 90% of the participants reported no sleep disturbance (Figure 7, p = 0.01).

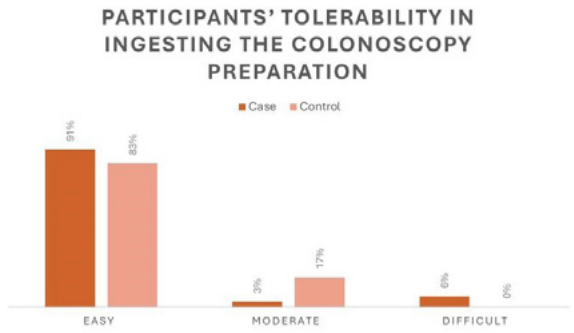

FIGURE 7 — Tolerance in ingesting bowel preparation

When investigating the prevalence of nausea and vomiting among participants, a higher incidence of these symptoms was observed in the splitdose group. Vast majority of participants either reported no symptoms or only mild symptoms. In the case group, approximately 20% experienced some degree of nausea. In the control group, about 17% reported mild nausea. Among all participants, only one individual in the split-dose group experienced syncope during preparation and required medical assistance. Abdominal pain, abdominal distension, and anal irritation were also evaluated through post-procedure questionnaires. Abdominal pain was reported by approximately 20% of participants who received the purgative on the morning of the exam, while about 15% of the control group reported some degree of abdominal pain (p=0.31). Regarding abdominal distension, both groups showed similar symptom rates (p=0.94). For anal irritation, a greater difference between the groups was noted (p=0.44); approximately 21% in the control group reported some degree of anal symptoms, compared to about 32% in the case group (Figure 8).

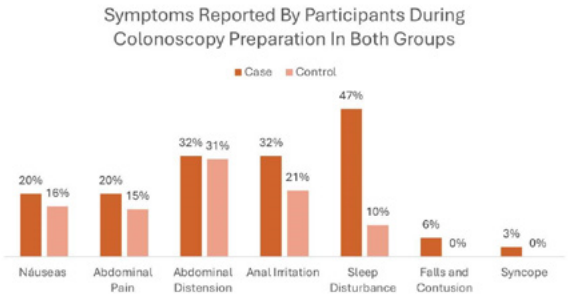

FIGURE 8 — Symptoms during bowel preparation for colonoscopy

DISCUSSION

Several studies have reinforced that split-dose bowel preparation regimens yield better outcomes in terms of both preparation quality and adenoma detection rate. A task force formed to standardize best practices in colonoscopy has reiterated that split-dose purgative regimens should routinely be implemented in services offering colonoscopy.[4]

The participants in the present study followed this same trend. Was observed that administering the purgative dose on the day of the exam improved the rate of adequate bowel preparation, according to the endoscopist's subjective assessment. However, the same improvement was not observed when using the BBPS as an isolated metric, where fewer participants in the split-dose group achieved a score ≥ 7 compared to the control group.

Sulfate-based solutions are osmotic purgatives widely used in bowel preparation for colonoscopy. In addition to being easy to use, they have minimal contraindications in patients with liver disease, congestive heart failure, or disorders related to electrolyte imbalance.

Another advantage of using split-dose sulfate-based purgative solutions is their greater tolerability, which has been consistently demonstrated in clinical practice. In a study evaluating colonoscopy preparation, polyethylene glycol was shown to be better tolerated than other methods, such as mannitol, with no significant difference in the final quality of bowel cleansing.[7]

In this study, only the purgative solution Picoprep® was used in 2 distinct groups, as previously described. Other types of bowel preparations, such as mannitol, were not evaluated. Both the purgative dose

administered on the day before the examination and the split-dose regimen were generally well tolerated. Vast majority of participants reported no symptoms when assessing nausea, vomiting, abdominal pain, bloating, and anal irritation. There was no statistically significant difference in tolerability between the two bowel preparation regimens, although participants in the split-dose group reported greater ease in following the instructions and a lower incidence of abdominal pain compared to those in the control group.

Another randomized clinical trial demonstrated the benefits of split-dose sulfate-based bowel preparation. There was a 15% increase in colonoscopies with excellent preparation quality compared to colonoscopies prepared with a single dose on the previous day.

Administering the purgative on the morning of the exam showed a trend toward a higher rate of colonoscopies with excellent preparation (BBPS score of 9). A total of 9 participants in the split-dose group achieved excellent bowel preparation, compared to 5 in the control group. The proportion of excellent preparations relative to the total was higher in the split-dose group— approximately 28%, compared to 26% in the control group.

It is recommended that the second dose of the purgative respects the necessary interval for the patient to undergo the examination, including travel time to the facility where the colonoscopy will be performed. According to Rex et al.[4,] the optimal timing for administering the second dose is between 3-8 h prior to the procedure.

However, a theoretical issue arises: The second dose may need to be taken very early, depending on the scheduled time of the examination. Nonetheless, clinical practice has shown that this early administration does not negatively impact the efficacy of bowel preparation, as evidenced by low rates of inadequate exams and high cecal intubation rates.

This observation was confirmed in this study. Was found that the cecal intubation rate (i.e., complete examinations with photographic documentation of the cecum) was higher among participants who received the split-dose regimen, despite a higher incidence of sleep disturbance: 94% in the intervention group vs. 81% in the control group. This is a relevant finding, as cecal intubation rate is considered a key quality indicator in colonoscopy. Complete examinations reduce the risk of interval colorectal cancer, particularly because incomplete exams fail to adequately evaluate the right colon.

Another important finding of this study relates to sleep quality. Sleep disturbances were significantly more frequent in the group that received the second dose of the purgative on the morning of the exam. In this group, participants took the second dose of Picoprep® between 5:00 and 7:00 AM, depending on the scheduled time of the procedure and ensuring a minimum interval of 3 h before the examination. This sleep interruption for laxative ingestion appears to be the main reason for the impaired sleep quality observed. There was a statistically significant difference between the groups regarding sleep disturbance during preparation (p=0.01): approximately 47% of participants in the intervention group reported some degree of sleep disturbance, compared to only 11% in the control group.

In the present study, the ADR was higher among participants who received a split-dose regimen, with the second dose administered on the morning of the procedure, compared to those who received the purgative only on the day before (p=0.36). Approximately 22% of participants in the intervention group had adenomas among the polyps detected, compared to around 16% in the control group. This study did not analyze ADR stratified by sex. The findings in the intervention group align with the recommendations of the most recent U.[5,] MultiSociety Task Force on Colorectal Cancer Screening, endorsed by the ACG.[4]

Despite the observed trend toward increased ADR with the addition of a second purgative dose on the day of the procedure, this difference did not reach statistical significance when compared to the control group. This may be partly explained by a higher dropout rate in the control group, which reduced its statistical power and representativeness.

Another important finding was the average size of polyps detected in both groups. Participants in the intervention group had smaller average polyp sizes than those in the control group. This may be attributed to the higher proportion of "excellent" bowel preparations (BBPS=9) in the intervention group. This observation is supported by findings from Repici et al.[8,] who demonstrated that colonoscopies with a BBPS score ≥ 8 enabled endoscopists to detect 100% of polyps larger than 5 mm. In contrast, in procedures with BBPS <7, only 88% of such polyps were detected. This finding has significant implications for patient outcomes and reinforces the clinical relevance of both the Boston scale and splitdose bowel preparation in routine CRC screening programs.

CONCLUSION

CRC has a high incidence and prevalence worldwide, and prevention remains the most effective strategy for reducing its impact. Therefore, assessing the quality of screening programs is essential. Bowel preparation using a split-dose purgative regimen administered on the day prior to the procedure is well supported by the literature and has proven to be effective. In this study, both the ADR and the cecal intubation rate showed a trend toward improvement in the group that received the split-dose regimen, compared to the control group. However, the high dropout rate in the control group may have affected the statistical significance of these findings. Tolerability was similar between the 2 regimens, although the split-dose preparation was associated with a higher frequency of sleep disturbances among participants.

Author´s contribution

Fabricio Grenteski – Conceptualization, Formal analysis
Laura Mendes Lopes – Investigation, Project administration
André Montes Luz – Supervision, Validation
Jurandir Marcondes Ribas Filho - Writing – review & editing, Methodology

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