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Comparison of patterns of laxative ingestion to improve bowel preparation for colonoscopy: a pilot randomized clinical trial *

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Authors

Adeyinka O. Laiyemo[1], Kolapo A. Idowu[2], Clinton Burnside[3], Carla D. Williams[3], Momodu Jack[1], Getachew Mekasha[1], Hassan Ashktorab[1], Hassan Brim[4], Edward L. Lee[4], Andrew K. Sanderson[5], Angesom Kibreab[1], John Kwagyan[6]

Institutions

1 Department of Medicine, Howard University College of Medicine, Washington, District of Columbia, United States
2 Department of Medicine, Johns Hopkins Medicine, Baltimore, Maryland, United States
3 Howard University Cancer Center, Washington, District of Columbia, United States
4 Department of Pathology, Howard University, Washington, District of Columbia, United States
5 Graduate School, Howard University, Washington, District of Columbia, United States
6 Georgetown-Howard Universities Center for Clinical and Translations Science, Washington, District of Columbia, United States

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Corresponding author
Adeyinka O. Laiyemo, MD, MPH, Division of Gastroenterology, Department of Medicine, Howard University College of Medicine, 2041 Georgia Avenue, NW, Washington DC 20060
Fax: +1-202-865-4607
adeyinka.laiyemo@howard.edu

ABSTRACT

Background and study aims Negative experiences with bowel preparation are a barrier to uptake of colonoscopy. The aim of this study was to examine the impact of different flavoring of polyethylene glycol (PEG) laxatives on patient satisfaction with and adequacy of bowel preparation during colonoscopy.

Patients and methods This was a single-blind (endoscopist), parallel design, randomized trial (NCT 02062112) during which patients scheduled for colonoscopy were assigned to one of three groups: Group 1 (no laxative flavoring, n = 84); Group 2 (flavored entire laxative, n = 90) and Group 3 (tasted PEG with and without flavoring and decided how they want to drink the rest of the laxatives (choice group), n = 82). Patients rated their bowel preparation experience (satisfaction) and endoscopists accessed adequacy of bowel preparation during colonoscopy.

Results There were no differences in patient ratings across the groups (1, 2 and 3) in taste of the laxatives ($P = 0.67$), ease of drinking ($P = 0.53$), and overall experience of bowel preparation process ($P = 0.18$). However, higher percentage of patients in the choice group would want the same laxative again if they were going to have a repeat colonoscopy in the future (72.5 % vs 81.3 % vs 88.9 %, $P = 0.04$). Surprisingly, adequacy of bowel preparation was highest among patients who drank their PEG unflavored (89.3 % vs 80 % vs 75.5 %, $P = 0.07$) and the had highest rates of adenoma detection (40.5 % vs 23.3 vs 39.0, $P = 0.03$).

Conclusions There were no differences in overall tolerability of bowel preparation by patterns of flavoring of PEG. Those who drank unflavored PEG were less satisfied but had better clinical outcome, suggesting minimum justification effect in bowel preparation process.

* **Meeting presentations**: An abstract from this study was presented at the American College of Gastroenterology Meeting in Honolulu, Hawaii in October 2015. [Am J Gastroenterol 2015; 110 (1): S567].

Introduction

Use of colonoscopy for colorectal cancer (CRC) screening has been increasing [1, 2]. Furthermore, colonoscopy is the diagnostic procedure to be performed when there is an abnormality detected by any other screening modality because of the opportunity to perform biopsies and remove polyps seen during the examination. However, colonoscopy requires full bowel preparation using oral laxative agents. The need for a complete bowel preparation process with dietary restriction and laxative ingestion can be a major barrier to undergoing colonoscopy for many patients. Lack of tolerability of the bowel preparation laxatives reduces the willingness to undergo colonoscopy and portends poor clinical outcomes including poor bowel preparation, missed colorectal lesions, and reduction in willingness to undergo future CRC screening.

Reduction in volume of laxatives to consume and flavoring of the laxatives have been undertaken with inconsistent results [3–8]. Furthermore, low-volume laxatives tend to be "non-preferred brands" for some third-party payers and they are generally associated with higher co-pays. Therefore, the 4 L polyethylene glycol (PEG), solution remains the major colonoscopy laxative used in many practices, especially among underserved populations with low socioeconomic status. Tolerability of this preparation is essential and it is the target of this study.

We hypothesized that patients would have a better experience if they tasted the bowel preparation laxative with and without flavoring and then decided how they wanted to drink the rest of the laxative since taste preferences vary widely from person to person. In this clinical trial, we investigated the effect of patterns of flavoring of laxatives on bowel preparation experience of patients undergoing outpatient colonoscopy and their clinical outcomes with adequate bowel preparation and subsequent adenoma detection.

Patients and methods

Study population

We recruited competent, non-institutionalized adult men and women who were scheduled for colonoscopy from gastroenterology clinics at Howard University from February 11, 2014 to September 10, 2014. The patients provided information on their demographic characteristics and lifestyle factors. All participants gave written informed consent and gave permission for their colonoscopy and pathology reports to be reviewed. The project was approved by the Howard University Institutional Review Board (IRB-13-MED-60). This was a pilot/feasibility project in preparation for a larger study to improve bowel preparation process and experience for outpatient colonoscopy. The investigators determined that approximately 100 participants in each arm would yield sufficient baseline data to guide subsequent studies.

Inclusion and exclusion criteria

We included adult patients who were scheduled for colonoscopy and gave informed consent. We excluded patients with a personal history of CRC and those at high risk for CRC as determined by history of familial adenomatous polyposis syndrome (FAP), family history of hereditary non-polyposis colorectal cancer syndrome (HNPCC), and personal history of inflammatory bowel disease (ulcerative colitis or Crohn's disease). Furthermore, we also excluded participants who had undergone bowel resection regardless of the indication for the surgery.

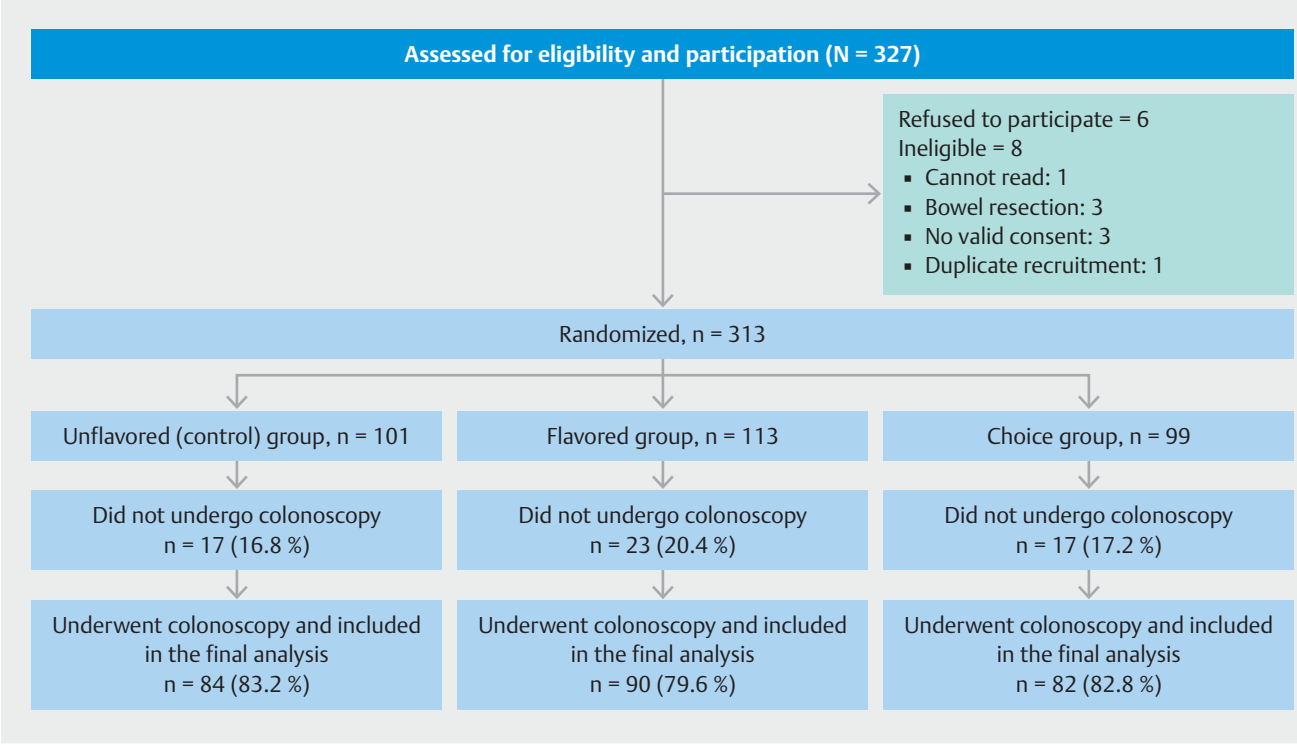
Randomization assignment

This was a single-blind (endoscopist), parallel design, three-arm pilot clinical trial. A total of 313 patients were randomly assigned to one of three groups using a computer-generated simple randomization sequence with instructions placed in sealed envelopes (concealed assignment). Group 1 patients (n = 101) were issued a gallon of PEG and were instructed to drink it without flavoring (unflavored group). Group 2 patients (n = 113) were issued PEG with flavoring packs (citrus or lemon per patient's preference) and were instructed to flavor the entire gallon and drink. Group 3 patients (n = 99) were issued PEG with flavoring packs but were instructed to taste a cup of PEG without flavoring and another cup with flavoring and decide for themselves how they wanted to drink the rest (choice group). A clear liquid diet the day before colonoscopy and split-dose bowel preparation were recommended for all patients. Of those randomized, those who completed the study by undergoing colonoscopy were group 1 (n = 84), group 2 (n = 90) and group 3 (n = 82) and constituted the primary analysis.

Outcome assessment

On the day of their colonoscopy, patients completed outcome forms detailing their bowel preparation experience (subjective assessment) using a rating scoring scale from 1 to 10 where (1 = unbearable; 5 = neutral; 10 = pleasant). Information gathered included their ratings of the bowel preparation laxative's taste, ease of consumption, presence or absence of nausea, actual vomiting, whether they consumed the entire recommended laxative, and their overall ratings of the bowel preparation experience. They were also asked whether they would like to have the same bowel preparation laxative if they needed colonoscopy in the future. Furthermore, they were asked whether they felt that their bowel was adequately clean for their colonoscopy (subjective assessment by patients).

During colonoscopy, the endoscopists who were all blinded to the randomization assignment of the patients rated the bowel preparation of the patients (objective assessment by endoscopists) using Aronchick scale selected in a drop-down menu format in their endoscopy reports. The bowel preparation was scored as poor, fair, good, very good or excellent as a function of how clearly the colonic mucosa was seen and the percentage examined clearly. Bowel preparation of poor and fair were considered as to be inadequate while good, very good and excellent designations were regarded as adequate bowel preparation. Findings of colorectal neoplasia were also recorded from the endoscopy and pathology reports.



▶ **Fig. 1** CONSORT diagram of flow of participants through the study. From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Statistical analyses

We compared baseline characteristics of the participants by randomization groups. We used chi squared test to compare the reported bowel preparation challenges of patients such as experience of nausea and vomiting by randomization arm. We compared subjective ratings of the patients' bowel preparation experience in terms of ease of drinking and taste of the laxatives using analysis of variance (ANOVA). We calculated and compared the percentage of patients with adequate bowel preparation as graded by the endoscopist in the colonoscopy reports. Adequate bowel preparation was defined as a description of good, very good or excellent on the Aronchick scale while inadequate bowel preparation was defined as fair or poor rating. The reference group for our analyses was the unflavored arm (group 1). We compared those issued with flavoring packs (group 2 and group 3) with group 1. We used log binomial models to compare the adequacy of bowel preparations and the presence of colorectal adenoma by randomization assignment. We calculated relative risks (RR) and 95 % confidence intervals (95 % CI). $P<0.05$ was regarded as statistically significant. We used Stata statistical software version 14.2 for all our analyses.

Results

Participant characteristics

A total of 313 participants were randomized (group 1 = 101; group 2 = 113 and group 3 = 99). Of them, 57 did not show up for their procedures or cancelled their colonoscopy appointments. Therefore, 256 (81.8 %) participants showed up for their procedures, underwent colonoscopy and were included in the final analysis (group 1 = 84; group 2 = 90 and group 3 = 82). CONSORT diagram (▶ **Fig. 1**) shows the flow of participants through the study. The characteristics of the subjects in the three arms were comparable (▶ **Table 1**).

Laxative drinking pattern of choice group participants (group 3)

Participants in group 3 (choice group) were issued flavor packets and were asked to taste the laxative flavored and unflavored and decide how they want to drink the rest of the laxative. Of 75 participants in this group who answered questions about how they eventually drank the laxative after tasting the flavored and unflavored options, 13 (17.3 %) participants drank the rest of the laxatives without flavoring while 53 (70.7 %) participants drank the rest with flavoring. The remaining nine participants (12 %) drank the rest of the laxative by flavoring some cups before drinking and drinking some cups of laxative without flavoring. However, we did not ascertain the exact percentage flavoring that they did.

Bowel preparation experience

There were no differences in ratings of the bowel preparation process across the randomization groups in terms of nausea, vomiting, drinking the entire laxative, taste of the laxatives, ease of drinking the laxatives, and overall experience with the bowel preparation process. However, a higher percentage of

▶ **Table 1** Characteristics of study participants.

Characteristics	Unflavored group (n = 84)	Flavored group (n = 90)	Choice group (n = 82)
Mean age in years (SD)	57.0 (10.0)	56.6 (8.5)	58.0 (9.9)
Sex, n (%)			
▪ Male	37 (44.0)	41 (45.6)	44 (53.7)
▪ Female	47 (56.0)	49 (54.4)	38 (46.3)
Black, n (%)			
▪ No	10 (12.4)	10 (11.8)	2 (2.7)
▪ Yes	71 (87.6)	75 (88.2)	72 (97.3)
Married, n (%)			
▪ No	59 (76.6)	61 (70.1)	48 (64.0)
▪ Yes	18 (23.4)	26 (29.9)	27 (36.0)
Highest education, n (%)			
▪ High school or less	47 (56.0)	52 (59.1)	49 (60.5)
▪ More than high school	37 (44.0)	36 (40.9)	32 (39.5)
Yearly household income, n (%)			
▪ More than $25,000	19 (23.5)	20 (25.0)	26 (33.8)
▪ $25,000 or less	62 (76.5)	60 (75.0)	51 (66.2)
History of smoking, n (%)			
▪ No	41 (49.4)	49 (55.7)	31 (38.8)
▪ Yes	42 (50.6)	39 (44.3)	49 (61.2)
Indication for colonoscopy, n (%)			
▪ Diagnostic study	45 (54.2)	46 (52.9)	42 (53.2)
▪ Colon cancer screening	38 (45.8)	41 (47.1)	37 (46.8)

those in the choice arm (group 3) reported that they would be willing to take the same laxative if they needed to undergo repeat colonoscopy in the future (▶ **Table 2**).

Adequacy of bowel preparation and adenoma detection

Overall, when asked if they felt that their colon was adequately clean for colonoscopy, 97.4% of all patients affirmed that their colon was clean without any difference by randomization arms: 96.3%, 97.4%, 98.7% for groups 1, 2, and 3, respectively (P = 0.64). This contrasts with an actual overall 81.6% adequacy of bowel preparation from endoscopic assessment. Adequacy of bowel preparation was highest at 89.3% among group 1 patients who drank the unflavored laxative when compared to 80% adequacy among group 2 patients who flavored all the laxatives and 75.6% among group 3 patients who tasted flavored and unflavored laxatives before making their choice about how they want to drink the rest (▶ **Table 3**). This represented a 15% reduced risk of adequate bowel preparation with the choice group 3 when compared to those who drank the entire laxative without flavoring. Adenomatous polyps were detected in 40.5% of patients in group 1, 23.3% in group 2 and 39.0% in group 3 representing a 42% statistically significant reduced risk of adenoma detection among those who flavored all the laxative as compared to group 1 patients who drank unflavored laxative (▶ **Table 3**). Adenoma detection was comparable among group 1 and group 3 subjects.

Discussion

It is well established that the bowel preparation process remains a major barrier to uptake of colonoscopy both as a screening modality and as a diagnostic tool in patient care. Efforts to improve patient bowel preparation experience can potentially increase uptake of colonoscopy among the population. In this study, we examined whether the pattern of flavoring can improve patient experience with attendant improvement in actual bowel preparation and adenoma detection at colonoscopy.

▶ **Table 2** Comparison of bowel preparation experience by randomization arm.

Experience	Unflavored group (n = 84)	Flavored group (n = 90)	Choice group (n = 82)	*P* value
Had nausea (yes)	23.5%	26.9%	30.3%	0.63
Vomited (yes)	3.7%	11.5%	10.5%	0.16
Drank entire laxative solution (yes)	88.9%	91.0%	89.5%	0.90
Thinks colon is adequately clean for colonoscopy (yes)	96.3%	97.4%	98.7%	0.64
Want the same laxative next time (yes)	72.5%	81.3%	88.9%	0.04
Mean rating of taste of laxative (SD)[1]	6.8 (2.8)	7.7 (2.5)	7.3 (2.6)	0.67
Mean rating of ease of consuming laxative (SD)	7.5 (2.4)	8.2 (2.2)	7.8 (2.4)	0.53
Mean rating of overall experience (SD)	7.9 (2.1)	8.1 (2.1)	7.9 (2.5)	0.18

[1] Using a rating scoring scale from 1 to 10 where (1 = unbearable; 5 = neutral; 10 = pleasant).

▶ **Table 3** Comparison of satisfaction with bowel laxative, adequacy of bowel preparation, and adenoma detection by patterns of flavoring of PEG.

Randomization group	% willing to have to have same laxative again	RR (95% CI)	% with good to excellent bowel preparation	RR (95% CI)	% with adenoma	RR (95% CI)
Unflavored	72.5	Reference	89.3	Reference	40.5	Reference
Flavored	81.3	1.12 (0.94–1.33)	80.0	0.90 (0.79–1.02)	23.3	0.58 (0.37–0.91)
Choice	88.9	1.23 (1.05–1.44)	75.6	0.85 (0.73–0.98)	39.0	0.96 (0.66–1.40)

Our study revealed that flavoring the bowel preparation laxative did not improve the overall experience for patients, but those who tasted unflavored and flavored solution and then decided how they would take the bowel laxatives (choice group 3) were more willing to have the same laxative if they needed to undergo colonoscopy in the future. Those who drank the unflavored laxatives were more dissatisfied and were the least likely to want to have the same laxative in the future if they needed to undergo colonoscopy. However, they had the highest adequacy of bowel preparation and subsequent highest percentage of adenoma detection. This suggests a minimum justification effect in the bowel preparation process.

Minimum justification is the phenomenon in which individuals rationalize overcoming some inconvenience to achieve small benefit at the individual level. Individuals use internal motivation to justify behavior. Drinking unpalatable unflavored PEG is an unpleasant activity in order to undergo an unpleasant procedure (colonoscopy) to prevent a rare event (colon cancer). Yet patients understand the need for this unpleasant activity and use their internal resources to ensure compliance, suggesting that people give themselves a positive reason for why they do what they generally do not want to do. Our study suggests that internal motivation of patients rather than merely more palatable taste of the laxative may play more of a role in terms of achieving adequate bowel preparation. Afterall, achieving adequate bowel preparation involves more than drinking laxatives because there are additional dietary modification and fluid ingestion requirements.

We are not aware of any study that has evaluated patterns of flavoring of PEG laxative to assess patient bowel preparation experience, actual bowel preparation and yield of adenoma at colonoscopy for direct comparison with our study. Nevertheless, our findings are comparable to the report of Hayes et al. [3] of their randomized control trial that involved 130 patients. The authors reported that flavoring the PEG solution did not make any difference in bowel cleansing with adequate bowel preparation occurring among 75% of participants who received flavored laxative and 76% among those who received unflavored laxative.

In another study which evaluated taste and volume of polyethylene glycol laxative use among patients scheduled for elective colonoscopy in the Netherlands, Szojda et al. [4] compared 3-L sulphate-free PEG (SF-PEG) and a 4-L PEG solution and evaluated patient acceptability and tolerability of the laxatives and effectiveness of the bowel preparation process among 102 patients who underwent colonoscopy. They reported that there were no differences in compliance, taste, tolerance and adequacy of bowel preparation. However, a statistically significant percentage of those who received the lower-volume solution expressed willingness to have the same laxative in the future.

For our study, we hypothesized that patients would have a better experience if they tasted the bowel preparation laxative with and without flavoring and then decided how they wanted to drink the rest of the laxative because taste preferences vary widely from person to person. Participants randomized to this choice arm had a more favorable opinion of the laxative in terms of taking it the next time if they needed colonoscopy in the future, but there was no difference in their tolerability of the bowel preparation process when compared to those who drank unflavored PEG, who were less likely to want the same laxative in the future. In contrast to our hypothesis, those in the choice group actually had lower adequacy of bowel preparation for their colonoscopy. The findings of Szojda et al. [4] and our study suggest that internal motivation to follow bowel preparation instructions probably has more impact on the adequacy of bowel preparation than the volume or taste of PEG. However, other studies suggested that 2-L PEG solution with ascorbic acid was noninferior to the 4-L PEG in bowel cleansing but was better in taste and compliance [5–7]. Therefore, there may be residual differences that could not be captured in our study. Furthermore, lower-volume laxative with better-tasting solutions may increase the willingness of patients to undergo colonoscopy in the future.

Another important finding of our study is the fact that participants grossly overestimated the adequacy of their bowel preparation for their colonoscopy. Subjective estimation by patients of their bowel preparation adequacy was 96.3%, 97.4% and 98.7% for groups 1, 2 and 3, respectively, whereas the objective bowel preparation adequacy from endoscopic examination was 89.3%, 80.0% and 75.6% for groups 1, 2 and 3, respectively. In fact, among six patients who opined that their bowel preparation mighty be less than optimal, four patients (66.7%) actually had adequate bowel preparation. This suggest that endoscopists should not rely on the positive estimation of bowel preparation adequacy from their patients.

A major strength of our study was that our randomized clinical trial was conducted among a predominantly underserved inner city minority populations who are frequently under-represented in biomedical research. Yet, our findings are comparable to those obtained among majority populations in the United States and studies conducted in other parts of the world. This suggests that improving the bowel preparation experience

of patients is a global necessity to reduce the burden of colorectal diseases including colorectal cancer in the world. Our study is limited by the relatively small number of participants. Therefore, it is possible that clinically relevant effects may be seen in larger studies. Nonetheless, the number of included patients in our study is larger than many previous studies on this important topic.

Conclusion

In conclusion, the patterns of flavoring of PEG laxative were not associated with improved tolerability of bowel preparation process for colonoscopy but those who tasted unflavored and flavored PEG and then decided how they wanted to drink the laxative were more willing to have the same laxative in the future. However, those who drank unflavored PEG were less satisfied but had better clinical outcomes in terms of adequacy of bowel preparation and subsequent adenoma detection, suggesting minimum justification effect in the bowel preparation process. The implication of this is that patients should be encouraged to use their internal motivation to overcome the lack of palatability they may experience in the course of undergoing the bowel preparation process for their colonoscopy.

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Clinical trial

Clinical.Trials.gov
NCT02062112
TRIAL REGISTRATION: single-center, single-blind (endoscopist), parallel design, prospective, three-arm randomized trial NCT02062112 at clinicaltrials.gov

Competing interests

The authors declare that they have no conflict of interest.

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