Efficacy of 1-day vs. 2-day intestinal preparation using PEG 3350 + Bisacodyl: A randomized clinical trial

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ABSTRACT

Objective. The objective was to compare the efficacy of 1-day intestinal preparation for colonoscopy using PEG 3350 (polyethylene glycol) (4 g/kg/day) + bisacodyl vs. 2-day intestinal preparation using PEG 3350 (2 g/kg/day) + bisacodyl in pediatric patients.

Materials and methods. A blind, randomized clinical trial was carried out with endoscopists who assessed colon cleansing. Patients aged 2-18 years old undergoing scheduled colonoscopy were included. They were randomized into 2 groups: 1-day preparation using PEG 3350 (4 g/kg/day) + bisacodyl, and 2-day preparation using PEG 3350 (2 g/kg/day) + bisacodyl. Endoscopic evaluation (Boston Scale) allowed the efficacy of both preparations to be assessed. Statistical analysis: T of Student for quantitative variables, and Chi square for qualitative variables.

Results. 72 patients with a mean age of 94 ± 49 months were included. No significant difference was found between groups regarding preparation difficulty and safety. Efficacy, assessed using the Boston Scale score and the proportion of excellent and good grades achieved, was higher in the 1-day group. Left colon score and total score were higher than in the 2-day group (left colon: 2.20 vs. 1.89, p=0.03; total score: 7.28 vs. 6.76, p=0.01) (left colon: 94.4% vs. 83.4%, p=0.034).

Conclusions. Efficacy in the quality of intestinal preparation for colonoscopy was higher in the 1-day group using PEG 3350 + oral bisacodyl than in the 2-day group.

KEY WORDS: Bisacodyl; Pediatric intestinal preparations; Polyethylene glycol.

EFICACIA DE LA PREPARACIÓN INTESTINAL CON UN DÍA DE PEG 3350 + BISACODILO EN COMPARACIÓN CON DOS DÍAS: ENSAYO CLÍNICO ALEATORIZADO

RESUMEN

Objetivo. Comparar la eficacia de la preparación intestinal para colonoscopia con 1 día de preparación con PEG 3350 (polietilenglicol) (4 g/kg/día) + bisacodilo en comparación con 2 días de preparación con PEG 3350 (2 g/kg/día) + bisacodilo en pacientes pediátricos.

Material y métodos. Se realizó un ensayo clínico, aleatorizado y cegado para los médicos endoscopistas que evaluaron la limpieza del colon. Se incluyeron pacientes de 2 a 18 años, que ameritaban colonoscopia en forma programada. Se aleatorizaron a los pacientes en dos grupos: 1 día de preparación con PEG 3350 (4 g/kg/día) + bisacodilo y 2 días de preparación con PEG 3350 (2 g/kg/día) + bisacodilo. Por medio de valoración endoscópica (escala de Boston) se determinó la eficacia de las dos preparaciones a evaluar. Análisis estadístico: T de *student* para cuantitativas y Chi2 para cualitativas.

Resultados. Se incluyeron 72 pacientes con edad promedio de 94 ± 49 meses. No hubo diferencia significativa entre los grupos con respecto a la dificultad y seguridad de la preparación. La eficacia, evaluada por el puntaje de la escala de Boston y la proporción de calificación excelente o buena, fue mejor en el grupo de un 1 día, el colon izquierdo y el puntaje total fue mejor en comparación al grupo de 2 días (colon izquierdo 2,20 *vs.* 1,89 p= 0,03 y total 7,28 *vs.* 6,76 p= 0,01) (colon izquierdo 94,4 *vs.* 83,4% p= 0,034).

Conclusiones. La eficacia de la calidad en la preparación intestinal para colonoscopia fue mejor entre el grupo de 1 día con PEG 3350 + bisacodilo vía oral en comparación a la preparación de 2 días.

PALABRAS CLAVE: Bisacodilo; Preparaciones intestinales pediátricas; Polietilenglicol.

INTRODUCTION

Colonoscopy is an endoscopic procedure carried out in children and adolescents to diagnose and treat various large bowel disorders, complemented with distal ileoscopy[(1)]. Ideally, preparation should free the colon from all fecal

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matter without causing histological disorders or hydroelectrolytic imbalances. It should be safe, comfortable, easily tolerable, and inexpensive[2].

For an adequate colonoscopy study, some basic quality requirements should be met in order to ensure maximum performance[3]. If preparation is inadequate, some areas will remain unexplored, so polypoid lesions, erosions, and vascular lesions will not be assessed, and most importantly, flat lesions will not be detected. Inadequate preparation is associated with incomplete mucosal evaluation, longer procedure times, increased complications, and patient discomfort owing to excessive insufflation[4].

The Boston Scale has been recently proposed to assess preparation quality in the various colon segments[5,6]. It evaluates the three colon segments (left, transverse, and right) based on their level of cleansing with scores ranging from 0 to 3, 0 being considered as an inadequate preparation, and 3 as an excellent preparation, with a maximum score of 9[6]. According to the literature, 23-50% of patients are not adequately prepared for examination, which leads to longer procedure times, incomplete examination, and study repetition[5,7-9].

The most widely used agents for colon preparation prior to colonoscopy include *bisacodyl* – which has a therapeutic action as a laxative by stimulating the nervous terminations in the intestinal wall, inhibits absorption, and increases water and electrolyte secretion[10] –, and *polyethylene glycol* (PEG 3350) – which leads to evacuations thanks to the mechanical effect of large volume lavage[11].

There are multiple barriers for an adequate intestinal preparation in children, including strict diets, bad taste, large liquid volumes, long preparation time, and adverse effects[12]. High doses and long preparations are associated with a cleaner colon, but may cause patient discomfort[13]. All preparations for colonoscopy can be associated with adverse events such as electrolyte disorders, dehydration, nausea, vomits, pain, hypoglycemia, and abdominal distension.

Some studies carried out in children have demonstrated 4-day intestinal preparations using PEG 3350 to be innocuous and effective, while some others have concluded that 1- day or 2-day preparations with 1.9 g/kg daily doses for two days, together with clear liquid diet, can also prove efficacious and harmless[7,10,14,15].

Today, there are no standardized preparation protocols for colonoscopy in children. There is a wide array of methods according to the healthcare facilities and the individual professionals involved. This lack of standardization makes it more difficult to determine the efficacy and safety of the various regimes available. The objective of this study was to compare the efficacy and safety of intestinal preparation for colonoscopy with 1-day preparation using PEG 3350 (4 g/kg/day) + 5 or 10 mg oral bisacodyl vs. 2-day preparation using PEG 3350 (2 g/kg/day) + 5 or 10 mg oral bisacodyl in pediatric patients aged 2-18 years old from our third level pediatric hospital.

MATERIALS AND METHODS

A controlled, randomized clinical trial was carried out with two types of colon preparations: *1-day preparation using PEG 3350 (4 g/kg/day) + bisacodyl, and 2-day preparation using PEG 3350 (2 g/kg/day) + bisacodyl*. From May 2016 to March 2018, children aged 2-18 years old consulting at the Gastroenterology Department and the Thoracic Surgery and Endoscopy Department of a third-level pediatric hospital were recruited.

Prior to study initiation, the protocol had been approved by the Hospital's Health Ethics and Research Committee. All parents had signed the relevant informed consent form.

Patients scheduled for diagnostic and/or therapeutic outpatient colonoscopy were included. Hospitalized patients and patients with emergency colonoscopy, colonic resection history, recent (< 28 days) intestinal surgery, known allergy to PEG or bisacodyl, chronic constipation causing fecal impaction, and decompensated renal, cardiac, or hepatic pathologies were excluded.

Randomization

The allocation to either of the study arms (1-day or 2-day) was random. The randomization process was performed before study initiation, through previously computer-generated random numbers. One member of the team was exclusively committed to delivering the specific maneuver for each patient in an opaque envelope according to randomization.

Procedures

Two types of procedures were carried out: 1-day preparation using PEG 3350 (4 g/kg/day) + bisacodyl, and 2-day preparation using PEG 3350 (2 g/kg/day) + bisacodyl. The dose and preparation procedure to cleanse the colon are thoroughly described in the publication of our study's preliminary results[16].

The efficacy of intestinal cleansing was the primary endpoint. It would be assessed using the Boston Scale, which evaluates cleansing quality by segments – left colon, transverse colon, and right colon (0 to 3 score for each colon section: Excellent=3, Good=2, Poor=1, Inadequate=0) – separately, and which allows a total score to be achieved by adding up the scores from the 3 segments. Scale assessment would be performed by two endoscopists unaware of which group each patient belonged to.

Two high-resolution videocolonoscopy devices were used: Fuji Film EC-530 MP/LP colonoscope, with an 11 mm external diameter, and Olympus CF-Q150L/I colonoscope, with a 12.8 mm external diameter. Colonoscopies were carried out by experienced endoscopists.

Secondary endpoints included assessing the maneuver's safety via a questionnaire to evaluate the presence of nausea, vomit, headache, and abdominal distension during intestinal preparation. In addition, prior to colonoscopy,

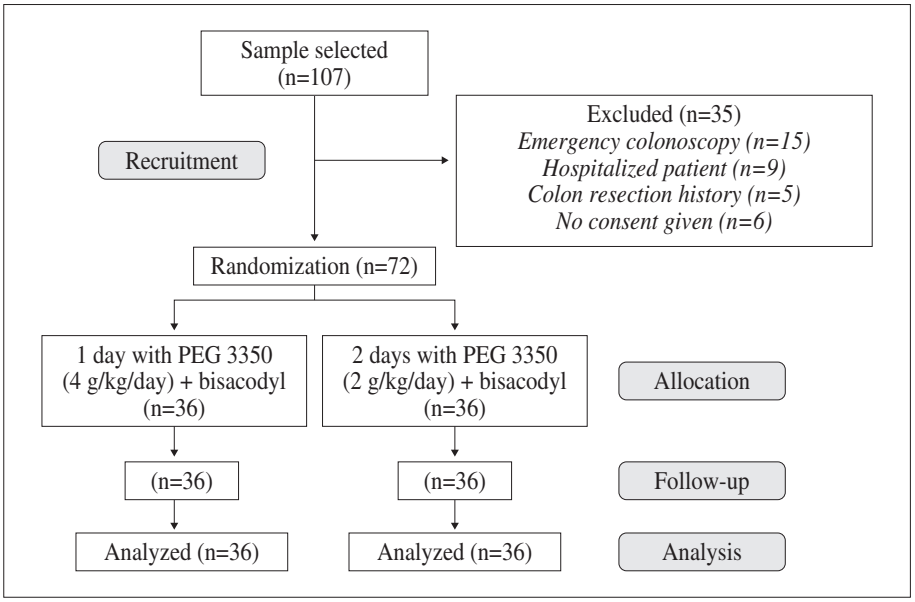

Figure 1.

a physical exploration was carried out to assess hydration, and a capillary glucose sample was obtained using an Accu-Check Performa glucometer.

Sample size was calculated using the data already published[16], with a difference in Boston Scale's score for the left colon of 2.41 ± 0.51 vs. 1.92 ± 0.73, a total 36 individuals per group, a 0.05 alpha level, and an 80% statistical power.

Statistical analysis

Dispersion and central tendency measures according to the variables' measuring scale. Quantitative variables were considered to have a distribution different from the norm, so they were normalized with their logarithm. To check whether descriptive variables were similar between groups, Fisher's exact test and T of Student test were used. Safety proportion between groups was assessed using Fisher's exact test. To compare Boston Scale score between groups, the T of Student test was applied. A $p<0.05$ value was considered significant. All analyses were carried out using the STATA software, version 12.0.

RESULTS

In the study period, a total 107 patients requiring colonoscopy were identified. A total 35 patients were excluded owing to various reasons: 15 of them required emergency colonoscopy, 9 were hospitalized, 5 had colon resection history, and 6 did not give their consent to take part in the study (Fig. 1).

The 72 patients meeting inclusion criteria were randomized. Mean age was 94 ± 49 months (2-17 years), with male patients representing 68.1% of the total sample. 75% of patients had low digestive tract bleeding history; this had an impact on colonoscopy, which demonstrated the presence of pathology in these patients (Table 1) (Fig. 1).

Age, sex, BMI z-score, constipation history, time from preparation to study, and pathological diagnosis at colonoscopy were compared in both groups, with no significant differences found, except for low digestive tract bleeding, which was more frequent in the 1-day group (86.1% vs. 69.4%, p=0.017) (Table 1).

PEG 3350 + bisacodyl intestinal preparation was administered to 100% of patients, none of them requiring nasogastric tube to complete the dose established. Following intestinal preparation administration, patients and their relatives were asked about the difficulty attached to preparation administration, with 11 patients (14.8%) defining it as difficult. Difficulty tended to be higher in the 2-day intestinal preparation group, but without significant differences between groups (1-day: 11.1%, n=4, vs. 2-day: 19.4%, n=7, p=0.32).

To evaluate safety, adverse effects such as nausea, headache, abdominal pain, and hypoglycemia were recorded. In the 1-day intestinal preparation group, 14 patients presented adverse events, while in the 2-day intestinal preparation group, 12 patients reported adverse events, with no significant differences between groups (Table 2).

When analyzing maneuver efficacy using the Boston Scale, left colon score and total score were higher in the 1-day colon preparation group than in the 2-day colon preparation group, with statistical significance (left colon: 2.20 vs. 1.89, p=0.03; total: 7.28 vs. 6.76, p=0.01). In addition, transverse colon and right colon scores tended to be higher in the 1-day colon preparation group than in the 2-day colon preparation group, with no statistical significance (Table 3).

Table 1. General patient data and comparison between groups.

	All n=72	*1-day n=36*	*2-day n=36*	
		n (%)		*p*
Age (months)+	94.1 ± 49.1	89.7 ± 41.5	98.2 ± 55.5	0.774
Male patients	49 (68.1)	25 (69.4)	24 (66.6)	0.550
BMI z-score+	0.15 ± 0.83	-0.01 ± 0.87	0.31 ± 0.77	0.123
Constipation	7 (9.6)	4 (11.1)	3 (8.3)	0.453
Reason for study: low digestive tract bleeding	56 (77.7)	31 (86.1)	25 (69.4)	0.017
Time from preparation to study	15.5 ± 1.2	15.2 ± 1.1	15.8 ± 1.3	0.087
Pathological diagnosis at colonoscopy	55 (75.3)	26 (72.2)	28 (77.7)	0.892

+Mean ± SD.

Table 2. Comparison of maneuver safety between groups.

	1-day n=36	*2-day n=36*	
	n (%)		*p*
Nausea	4 (11.1)	5 (13.8)	0.536
Headache or abdominal pain	7 (19.4)	2 (5.5)	0.064
Hypoglycemia	3 (8.3)	5 (13.8)	0.387

Efficacy was also assessed using the Boston Scale by comparing the proportion of individuals with an excellent or good colon cleansing grade. In the case of the left colon, there were more patients with an excellent or good grade in the 1-day preparation group than in the 2-day preparation group, with statistical significance (94.4% vs. 83.4%, p=0.034) (Table 3).

DISCUSSION

1-day intestinal preparation was found to be more effective than 2-day intestinal preparation. In general, both preparations for colonoscopy had adverse effects, without significant differences between groups.

Intestinal preparation protocols vary largely in terms of length and drugs used. However, the shorter the preparation, the less upsetting for patients, and therefore, the higher adherence to this maneuver. This is why, in the last years, multiple prospective studies have been carried out in pediatric patients to demonstrate that colon cleansing is similar in short and long schemes[14,15,17-19], with controversial results.

For example, Phatak U et al. used PEG 3350 + bisacodyl for 2 days, with an excellent or good reported cleansing quality in the right and left colon of 92% and 93%, respectively. In our study, in the case of the right colon, the 2-day preparation had an excellent or good quality in 83.4% of patients, which is lower than the proportion noted by Phatak U, whereas the 1-day preparation had an excellent or good quality in 94.4% of patients, similar to the number reported by Phatak U. On the other hand, in the case of the left colon, the 2-day preparation had an excellent or good quality in 97.3% of patients, whereas the 1-day preparation had had an excellent or good quality in 100% of patients, both numbers being higher than those reported by Phatak U[17].

Other studies have compared colon preparation with PEG only, finding fewer patients with excellent cleansing, and lower Boston Scale scores than in our study. For instance, Najafi et al. evaluated 2 colon preparations with PEG, with an excellent and good efficacy in the 1-day preparation (70%) and in the 2-day preparation (72%). However, the proportion was higher in our study (1-day: 94.4%, and 2-day: 83.4%)[14]. Similarly, Abbas et al.[18] reported a mean total score of 6.16 in the Boston Scale, which was also lower than in our study (global Boston Scale of 7.28 in the 1-day group, vs. 6.76 in the 2-day group). The additional stimulating effect of bisacodyl may have played a role in this, since it was used in both groups, regardless of the amount of PEG administered to patients.

Adverse effects reported by Phatak U et al.[17] included nausea (19%), abdominal pain (11%), and vomit (4%), the three of them being mild. Najafi et al.[14] reported abdominal pain and nausea, with no significant differences between study groups. Abbas et al.[18] reported nausea or vomit (60%), abdominal pain or colics (44%), and weakness or fatigue (40%). Adverse effects identified in our study were similar to those described by these authors, with headache, abdominal pain, nausea, and vomit, all of them being mild. Adverse effects were recorded in 36.1% of patients (n=26), with no difference between groups. None of the patients presented dehydration, and 11.1% (n=8) had hypoglycemia, with a higher proportion in the 2-day group, without statistically significant differences.

Table 3. Comparison of maneuver efficacy between groups using the Boston Scale.

		1-day n=36	*2-day n=36*
		mean ± SD	
Score	Left colon*	**2.20 ± 0.53***	**1.89 ± 0.68***
	Transverse colon	2.48 ± 0.50	2.35 ± 0.53
	Right colon	2.57 ± 0.69	2.53 ± 0.55
	Total	**7.28 ± 1.12***	**6.76 ± 1.36***
		n (%)	
Left colon*	Excellent	**10 (27.8)**	**10 (27.8)**
	Good	**24 (66.6)***	**20 (55.6)***
	Poor	**2 (5.6)***	**6 (16.6)***
	Inadequate	**0 (0)**	**0 (0)**
Transverse colon	Excellent	18 (50)	14 (38.5)
	Good	18 (50)	21 (58.8)
	Poor	0 (0)	1 (2.7)
	Inadequate	0 (0)	0 (0)
Right colon	Excellent	24 (66.6)	20 (55.6)
	Good	10 (28)	15 (41.7)
	Poor	1 (2.7)	1 (2.7)
	Inadequate	1 (2.7)	0 (0)

**p<0.05.*

Although no differences were found between groups in terms of intestinal preparation's administration difficulty, a tendency to lower difficulty was noted in the 1-day preparation group. This is consistent with other studies, where shorter preparation times proved better for patients[19]. In light of this, it could be stated that the shorter the preparation, the better for patients and clinicians regarding preparation adherence.

In terms of potential confusion variables, both groups had similar results. Regarding constipation diagnosis, based on Rome IV criteria, the proportion in the 1-day group was 11.1% vs. 8.3% in the 2-day group. In addition, time from preparation completion to study initiation in the 1-day group was 15.2 ± 1.2 hours vs. 15.8 ± 1.3 hours in the 2-day group, without statistically significant differences.

Our primary study limitation lies in the fact that most cases had low digestive tract bleeding. However, most colonoscopies in our department are carried out precisely because of this, with very few being associated with other pathologies. In addition, given that our patients were outpatients, intestinal preparation adverse effects were subjectively assessed – for instance, abdominal distension should have been evaluated by measuring waist perimeter.

It is worth noting that, although the assessment of colon cleansing results using the Boston Scale is associated with a <0.05 p value (1-day: 7.28 ± 1.12 vs. 2-day: 6.76 ± 1.36), this is actually a little clinical magnitude.

CONCLUSIONS

In pediatric patients aged 2-18 years old, the efficacy of intestinal preparation for colonoscopy was higher in the 1-day group using PEG 3350 + oral bisacodyl than in the 2-day group. No differences were found between groups in terms of tolerance and safety.

Therefore, we advocate the use of the 1-day preparation, which will also be more comfortable for patients and their parents.

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