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BRIEF ARTICLE

Polyethylene glycol 3350 based colon cleaning protocol: 2 d *vs* 4 d head to head comparison

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Abstract

AIM: To compare between 2 and 4 d colon cleansing protocols.

METHODS: Children who were scheduled for colonoscopy procedure (2010-2012) for various medical reasons, were recruited from the pediatric gastroenterology clinic at Marshall University School of Medicine, Huntington, WV. Exclusion criteria were patients who were allergic to the medication used in the protocols [polyethylene glycol (PEG) 3350, Bisacodyl], or children with metabolic or renal diseases. Two PEG 3350 protocols for 4 d (A) and 2 d (B) were prescribed as previously described. A questionnaire describing the volume of PEG consumed, clinical data, and side effects were recorded. Colon preparation was graded by two observers according to previously described method. Main outcome measurements: Rate of adequate colon preparation.

RESULTS: A total of 78 patients were considered for final calculation (group A: 40, group B: 38). Age and stool consistency at the last day was comparable in both groups, but the number of stools/day was significantly higher in group B (P = 0.001). Adequate colon preparation was reached in 57.5% (A) and 73.6% (B), respectively (P = 0.206). Side effects were minimal and comparable in both groups. There was no difference in children's age, stool characteristics, or side effects between the children with adequate or inadequate colon preparation. Correlation and agreement between observers was excellent (Pearson correlation = 0.972, kappa = 1.0).

CONCLUSION: No difference between protocols was observed, but the 2 d protocol was superior for its shorter time. Direct comparison between different colon cleansing protocols is crucial in order to establish the "gold standard" protocol for children.

Key words: Colonoscopy; Polyethylene glycol 3350; Cleansing protocol; Children

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INTRODUCTION

Colon cleansing protocols have been one of the limiting factors in preparing children for diagnostic colonoscopy procedures needed for various medical reasons. Due to bad palatability and the quantity needed, the commonly used liquids in adult patients are not accepted by children and compliance is unacceptable[1-3]. In the last decade, polyethylene glycol (PEG) 3350 has been introduced to children and was found to be palatable and acceptable by children for the treatment of various medical conditions, mainly constipation. Several studies have shown that children will accept this PEG based solution and the compli-

ance rate was very good even for long term therapy[4-7]. In the past, we showed that PEG 3350 is an excellent solution for colon cleansing protocol in children reaching adequate colon preparation in up to 92% of the children examined[8]. Moreover, we reported that following the number of defecation and stool consistency in the last days of preparation may be used as indicators for the colon condition, and would reduce the number of failed procedures due to an unprepared colon. In recent years a similar PEG 3350 based protocol was reported that suggested similar results with a shorter preparation[9]. In that protocol, a higher dose of PEG 3350 with daily dose of 5 mg Bisacodyl resulted in an excellent colon condition for colonoscopy reaching up to 92%[9].

An unprepared colon in adults is considered one of the limiting factors for achieving an adequate rate of polyp detection during colonoscopy procedures[10,11]. In children, the rate of the unprepared colon during colonoscopy is high and was reported between 5%-30%[12-15]. The different colon cleansing protocols used by different centers was never standardized and the "optimal" protocol has never been established. We believe that a head to head comparison between protocols in children is needed in order to standardize clinical practice and to find the best available protocol. Such protocol would limit the rate of the unprepared colon and established the gold standard protocol for colonoscopy procedures in children.

In the present study, in a head to head analysis, we prospectively compare two different PEG 3350 based protocols in order to establish the better cleansing protocol in children.

MATERIALS AND METHODS

Children who were scheduled for colonoscopy procedure (2010-2012) for various medical reasons, were recruited from the pediatric gastroenterology clinic at Marshall University School of Medicine, Huntington, WV. Exclusion criteria were patients who were allergic to the medication used in the protocols (PEG 3350, Bisacodyl), or children with metabolic or renal diseases. One of the two different colon protocols was prescribed to the participating patients. A computer generated random list assigned the children to each protocol. The parents/caregivers (or child when appropriate) were asked to complete a clinical questionnaire during the colon preparation as previously described[8]. Briefly, the questionnaire included the amount of PEG 3350 consumed per day, number of stools per day, consistency of stool (scale: 1-5), and various side effects (abdominal pain, vomiting). Informed consent was obtained from all participants and the study was approved by the IRB Committee at Marshall University School of Medicine, Huntington, WV.

Colon cleansing protocols

Two PEG 3350 protocols for 4 and 2 d were prescribed as previously described[8,9]. The 4 dy protocol (protocol A) included PEG 3350 at 1.5 g/kg per day (up to a limit of 100 g/d) for 4 d. Patients were allowed to eat regular food until the day before procedure and clears only at the last day of protocol. The 2 d protocol (protocol B) included PEG 3350 at 2 g/kg per day (up to a limit of 136 g/d) plus 5 mg/d Bisacodyl for 2 d. Patients were allowed to eat regular food on day 1 and clears on day 2. No adjunct medication or enema was allowed in any of the protocols. The parents/caregivers were required to complete a simple questionnaire as previously described[8]. The questionnaires were returned to the physicians on the day of procedure and reviewed with the parents to ensure compliance and accuracy. Patients who did not follow the protocol for various reasons including: inadequate PEG 3350 dose, missed clinical data on the questionnaire, or other protocol violations, were excluded from the final calculation.

Colon preparation assessment

Colonoscopy procedure was performed under propofol sedation given by certified anesthesiologists. The colon was assessed according to previous methodology as previously described[8]. Briefly, the colon preparation was graded according to 5 different levels (Grade 1 to 5) as follows: G1: unacceptable (large amount of solid stool covering the mucosa); G2: poor preparation (enough stool that much of intra-procedural cleaning was required); G3: fair preparation (some liquid stool, easily removed); G4: good preparation (successful visualization of the colon mucosa); G5: Excellent preparation (Crystal clear colonic mucosa). For the current study, colon preparation at grade $\geqslant$ 4 was considered as adequate colon preparation. The investigators were allowed to incorporate 0.5 grade per their discretion. Grading of colon preparation was performed within 5-10 min of procedure completion. To reduce bias, the grading was performed simultaneously and separately by the endoscopist (Elitsur Y), and the assisting endoscopy nurse who participate in the procedure (Butcher L). The grading was documented on a separate page where both persons were blinded to the documentation of the other. Once documentation was done, both grades became final and no change of grading was allowed. A correlation between physician's grade and the nurse's grade was calculated.

Statistical analysis

Comparison between the two protocols was performed using two-tailed χ^2 analysis, and nonparametric analysis (Wilcoxon Signed Rank Test) using the IBM-SSPS statistics 19 program. Correlation analysis was performed using Pearson correlation. Significant analysis was set at P value < 0.05.

RESULTS

A total of 93 children enrolled (period 2010-2012), of whom 48 were assigned to protocol A and 45 to protocol B. A total of 15 patients were not included in the study due to a protocol violation, 8 in protocol A and 7 in pro-

Table 1 Clinical data

Protocol	4 d	2 d	*P* value[1]
No patients	40	38	
Age (yr, mean ± SD)	10.10 ± 4.6	9.91 ± 4.7	0.792
Male/female ration	1.0:1.0	0.8:1.0	0.811[4]
No stools/d (mean ± SD)[2]	5.15 ± 2.6	7.88 ± 4.1	0.001
Consistency (mean ± SD)[2]	5.65 ± 0.8	5.49 ± 0.9	0.904
Colon grade (mean ± SD)	3.50 ± 1.1	4.01 ± 1.0	0.140
Colon grade (≥ 4)[3]	23 (57.5%)	28 (73.6%)	0.206[4]

[1]*P* value: wilcoxon signed rank test; [2]At the last day of protocol; [3]Grade ≥ 4 considered adequate preparation; [4]*P* value: χ^2 analysis.

tocol B. The major clinical diagnoses were gastrointestinal bleeding of unknown origin, and follow up colonoscopy in inflammatory bowel disease patients. Overall, a total of 78 patients were considered for final calculation, 40 in protocol A and 38 in protocol B. In both protocols, the number of stools per day increased from the first day to the last day of protocol (data not shown). The age, male/female ratio, and stool consistency at the last day in either protocol was comparable for both groups, but the number of stools per day was significantly higher in group B compared to group A (Table 1). Adequate colon preparation (defined as grade ≥ 4) was reach in 57.5% and 73.6% of children from protocol A and protocol B, respectively (P = 0.206, Table 1). Side effects were minimal and comparable in both groups (abdominal pain: 26%-32%, vomiting: 2%). None of the children discontinued his protocol due to side effects. The cecum was successfully reached in 76 (98%) children, and when attempted, the terminal ileum was visualized in 68 (87%) children (32 children in protocol A and 36 children in protocol B). There was no difference in children's age, stool frequency, stool consistency, or side effect between the children who had adequate colon preparation (grade > 4.0) and those with inadequate colons (grade < 4.0) (data not shown). The correlation and agreement between colonoscopy grading between physician and the endoscopy nurse for both groups was excellent (P = 0.972, kappa = 1.0).

DISCUSSION

Preparing the colon for colonoscopy procedure for children has been a difficult task for many years, and various colon cleansing protocols have been suggested and used. In fact, there is no one pediatric protocol that has been accepted as the "gold standard" and different medical centers are using different protocols. In some centers, the adult protocol is used for teenage children and young adults. After we confirmed the excellent results with a 4 d PEG 3350 protocol, it became the preferred colon cleansing protocol in our clinic[8]. In 2011, Phatak *et al*[9] presented a similar PEG 3350 based colon preparation protocol that was shorter. In the present study, we present for the first time a true head to head comparison between 2 different colon cleansing protocols in order to establish the better protocol for children. Results showed that both protocols were comparable with regard to the rate of adequate colon preparation, stool characteristics, side effects, or patients' compliance. The number of stools per day at the last day of the shorter protocol (protocol B) was significantly higher compared to protocol A (P = 0.001), but no difference in the colon grading was noted between the groups. In fact, the adequate colon preparation, as defined in our study (grade ≥ 4), was higher in protocol B but did not reach a statistical significance (57.5% *vs* 73.6%, P = 0.206). We believe that the addition of a stimulant laxative (Bisacodyl), and the higher dose of PEG 3350 prescribed in protocol B (1.5 g/kg *vs* 2.0 g/kg) were the reasons for those results. We suggest that the 2 d protocol is at least as good as the 4 d protocols while having the advantage of being a shorter protocol.

We acknowledge the few differences existed in our study. (1) When compared with previous reports, our study showed a lower rate of adequate colons in both groups (57.5% and 73.6% for protocols A and B, respectively). In the present study we followed a stricter definition for adequate colon preparation (grade ≥ 4.0) that may reduce the rate of success in our population. When the definition of adequate preparation dropped to grade ≥ 3.5, our success rate increased to 63% and 79%, respectively (P = 0.17). Similarly, when a higher degree of preparation (excellent preparation) was considered in Phatak's study[9], a comparable rate of adequate colon was achieved between both studies; (2) Compared with previous study[9], a second observer (gastrointestinal nurse), blinded to the grading of the first observer, was utilized to grade the colons. The agreement between both observers was excellent (Spearman correlation = 0.972, kappa = 1.0); and (3) The number of participants in our study was lower than in previous studies, a fact that could explained the lack of statistical significance noted between the protocols[8,9]. We suggest that those methodological differences may explain the lower rate of adequate colon preparation reported in our study.

In conclusion, we prospectively compared two PEG 3350 based cleansing protocol for children who were scheduled for diagnostic colonoscopy. Our results showed that both protocol were acceptable to children, but the 2 d protocol is superior to the 4 d protocol at least for its shorter course. Further comparison between different cleansing protocols in children is needed in order to establish the best protocol for colonoscopy procedure in children.

COMMENTS

Background

Colon cleansing protocols have been the major obstacle in successful colonoscopy in children. Of the polyethylene glycol (PEG) 3350 protocols published, none has been recommended as the best protocol.

Research frontiers

In the last decade, PEG 3350 has been introduced to children and was found to be palatable and acceptable by children for the treatment of various medical

conditions, mainly constipation. Several studies have shown that children will accept this PEG based solution and the compliance rate was very good even for long term therapy.

Innovations and breakthroughs

In recent years a similar PEG 3350 based protocol was reported that suggested similar results with a shorter preparation. In that protocol, a higher dose of PEG 3350 with daily dose of 5 mg Bisacodyl resulted in an excellent colon condition for colonoscopy reaching up to 92%.

Applications

In the present study, in a head to head analysis, the authors prospectively compare two different PEG 3350 based protocols in order to establish the better cleansing protocol in children.

Peer review

The number of stools per day at the last day in each protocol, and the mean colon grading was significantly higher in the shorter protocol (protocol B). This is a randomized controlled trial and an interesting and important paper for colonoscopy procedures in children.

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