A Randomized Trial of Enema Versus Polyethylene Glycol 3350 for Fecal Disimpaction in Children Presenting to an Emergency Department

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Objective: This study aimed to compare efficacy of enema versus polyethylene glycol (PEG) 3350 for pediatric fecal impaction treatment.
Methods: We conducted a prospective, randomized comparison of treatments of fecal impaction in children in a pediatric emergency department (ED). Treatment arms were a single milk and molasses enema in the ED or PEG 3350 for 3 days outpatient. Telephone follow-up was done on days 1, 3, and 5. The primary outcome was main symptom improvement. Additional outcomes were stool frequency, consistency, and ease of stool passage. Treatment failures (home enema, ED return, or hospital admission) were tracked.
Results: Seventy-nine subjects participated (39 PEG; 40 enema). At day 1, PEG subjects were less likely to have improved main symptom (odds ratio [OR], 0.3; 95% confidence interval [CI], 0.1–0.8) but no difference in other outcomes. Half (54%) in enema arm were reported as upset by ED therapy, whereas no children in PEG arm were upset ($P < 0.05$). At day 3, more patients in enema arm reported ideal stool consistency (74% vs 38%; $P < 0.05$). At day 5, no difference between groups was noted. Most treatment failures were in PEG arm (83%; $P = 0.08$).
Conclusions: This pilot study suggests that disimpaction by enema may be superior to PEG for immediate relief of symptoms. Larger trials are needed to assess any advantage.

Key Words: fecal impaction, constipation, enema, randomized trial

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Constipation is a common childhood condition and is defined by the ROME II criteria as scybalous, pebble-like, hard stools for most stools; or firm stools for twice or less per week.[1] In most children, constipation is functional, occurring without evidence of a pathological condition. Constipation and fecal impaction can cause a range of symptoms from decreased appetite to abdominal pain and is frequently diagnosed in children evaluated in the emergency department (ED).[2–5]

General guidelines for constipation treatment include fecal impaction removal before initiation of maintenance therapy with behavioral interventions and laxatives.[2,6–9] Disimpaction may be performed using various oral therapies (including polyethylene glycol [PEG] 3350); however, rectal therapies such as enemas are frequently used, especially in the ED/urgent care setting.[4,10–12] PEG 3350 (Braintree Laboratories Inc, Braintree, Mass) is a tasteless, dissolvable osmotic agent that acts to increase fecal water content and is widely used in clinical practice. Several studies have established dosing guidelines and demonstrated safety and efficacy for children.[11,13–18] Although both oral and rectal therapies are accepted as treatment of impaction and constipation, there is only one published randomized study that compares the 2 modalities.[19]

Few studies describe constipated children treated in an ED. We recently described practice variation and patient response in our pediatric ED and found that enemas were used in 30% of constipated patients, and most (74%) were discharged with a laxative.[4] Although older children were more likely to have short-term improvement, many children treated for constipation continued to have symptoms regardless of presenting symptoms, treatment, or sex.[4] Similar to a previous study, we found that the use of enemas in the ED did not influence short-term symptom resolution.[5] Recently, enema was compared to PEG 3350 for treatment of fecal impaction; subjects were treated for 6 consecutive days and treatments were found to be equally effective.[19]

Because of a paucity of randomized trials, many of the guidelines for treatment of fecal impaction and functional constipation are not evidence based.[20] Our study aimed to compare the efficacy of PEG 3350 to enema for improvement of symptoms in children with fecal impaction and constipation treated in a pediatric ED.

METHODS

Study Design

We conducted a single-site, randomized clinical trial of milk and molasses enema versus oral PEG 3350 for treatment of fecal impaction, functional fecal retention, or excessive colonic stool in constipated children aged 1 to 17 years. The institutional review board approved the study, and all study parents/guardians provided written informed consent with children providing assent when appropriate.

Study Setting

This study was conducted in the ED of a free-standing, academic children's hospital located in the midwestern United States. The annual volume exceeds 65,000 patients.

Study Protocol

Participants

A convenience sample of patients aged 1 to 17 years was recruited between December 2006 and May 2009. A diagnosis of at least one of the following by the treating ED physician was required to be eligible: (1) fecal impaction (lower quadrant mass or dilated rectum with hard stool), (2) functional fecal retention

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The manufacturer label states that the safety and efficacy for Polyethylene Glycol 3350 has not been established for pediatric patients.
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(large diameter stools as determined by caregiver for less than twice per week and retentive behaviors), or (3) excessive stool in colon on abdominal radiograph as determined by radiologist or treating ED physician. Exclusion criteria included patients who had milk or molasses allergy, were ill-appearing (determined by treating physician), received analgesia for abdominal pain (except acetaminophen or ibuprofen), had diagnostic testing beyond plain radiographs or urinalysis, had prior abdominal or rectal surgery, were non-English speaking, were pregnant, had long-term medical conditions that may be associated with constipation (ie, cystic fibrosis, cerebral palsy, hypothyroidism, spinal, and gastric anomalies), or were admitted to an inpatient service.

Randomization

To ensure equal distribution of treatments among different ages, block randomization was used for 3 age groups (1–4, 5–10, and 11–17 years), and a list assigning participants to a treatment arm was randomly generated by a computer, in blocks of 10. The results of the randomization were not revealed until just before treatment was initiated. Because of obvious differences in the treatment arms (oral vs rectal medication), blinding of the participants and study personnel was not possible.

Baseline Data

Before receiving an intervention, caregivers of subjects provided information on demographics and past medical history. Additionally, baseline data were collected from caregivers (and participants if appropriate) using questions from the Questionnaire on Gastrointestinal Symptoms (QGS).[21] The QGS instrument is now widely used to classify children's gastrointestinal symptoms into diagnostic groups. Development of this instrument was a collaborative effort that underwent multiple pilot tests and revisions.[21] The QGS also allows for assessment of post–intervention symptoms and was used in modification for follow-up as well.

Intervention

Participants were randomized to a single milk and molasses enema in the ED (mixed 1:1, 10 mL/kg with maximum 500 mL, standard enema therapy at this institution) or oral high-dose PEG 3350 (1.5 g/kg/d, max dose of 100 g/d) for outpatient use for 3 days.[11]

Subjects in both groups were discharged with PEG 3350 for maintenance therapy (at 0.8 g/kg/d for 3 days)[22]; enema subjects were instructed to start maintenance within 24 hours after ED discharge and PEG 3350 subjects advised to start within 24 hours after taking the third cleanout dose. Participants received written instructions on their cleanout and maintenance regimens and also received enough complimentary PEG 3350 to complete this study. Subjects received additional, standard discharge information on constipation from the treating ED physician.

Follow-Up

Primary caregivers were contacted by telephone for follow-up on days 1, 3, and 5 to evaluate stool patterns, on-going symptoms, and symptom improvement. Structured surveys were conducted by the primary investigator (M.M.) or a research assistant and took 5 to 10 minutes to complete. Because of the difficulty in obtaining follow-up, we accepted responses up to 7 days after enrollment. If caregivers believed the subject was not tolerating the study treatment, they were instructed to contact the research coordinator (who would advise over-the-counter sodium biphosphate/sodium phosphate enema treatment or physician evaluation after consulting with a study principal investigator). Treatment failure was defined as a participant who received an enema at home, returned to the ED for evaluation, or was later admitted to an inpatient service for treatment of fecal impaction.

Data Analysis

Measurements

Similar to previous studies, the main outcome measure was the change in the child's main symptom.[4,5] Changes were determined by the question "Has your child's main symptom improved, stayed the same or gotten worse?" The main symptom was defined as the chief complaint identified during the triage process. For analysis, responses were dichotomized into 2 groups: improved/better versus worse/same.

Additional outcomes measured included straining with stools, stool consistency, and stool pattern (using modified questions from the QGS[21]). Straining with stool passage was assessed by the question "Does your child have to strain (push hard) to make a bowel movement come out?" For analysis, responses were dichotomized into 2 groups: Yes versus No/Not applicable (no stool). Stool consistency was assessed by the question "What have most of your child's bowel movements been like?" Responses were dichotomized into groups: those with ideal consistency answered "not too hard and not too soft" or "very soft or mushy" and others answered "very hard," "hard," or "watery." Questions about stool regularity were asked only after all patients had completed their cleanout phase (on days 3 and 5 only).

Subjects for whom follow-up data were not available and subjects who answered "don't know" were omitted from analysis. A χ^2 test was used to examine the difference in probabilities of experiencing an outcome between treatment arms and differences were expressed by Mantel-Haenszel common OR estimate with 95% confidence interval (CI). Independent samples t test were used to compare means for stool output between treatment arms.

This study was registered with the National Institutes of Health at www.clinicaltrials.gov (study identifier = NCT00467350) and we followed the most recent CONSORT statement for reporting our data.[23] The data were analyzed using SPSS statistical software (SPSS Inc, Chicago, Ill).[24]

Sample Size Analysis

Initially, we calculated that treatment of 70 patients in each arm would provide 80% power for detecting a change of 25% versus 50% in the 2 groups on day 5 (proportion of patients who respond "improved" to the question "Has your child's main symptom improved, stayed the same or gotten worse?"). This assumed a two-sided α level of 0.05 and approximately 12 patients lost to follow-up in each arm. However, we became concerned that patients in the oral cleanout arm were experiencing an inferior outcome so the decision was made to analyze the data we had collected to date (before obtaining 140 total patients).

RESULTS

Patient flow into the study is described in Figure 1. Of the 169 patients approached, 80 (47%) were enrolled; 39 were randomized to the oral cleanout arm and 41 to the enema arm (1 withdrew after consent but before treatment). There was no significant difference in sex between refusals and enrollees;

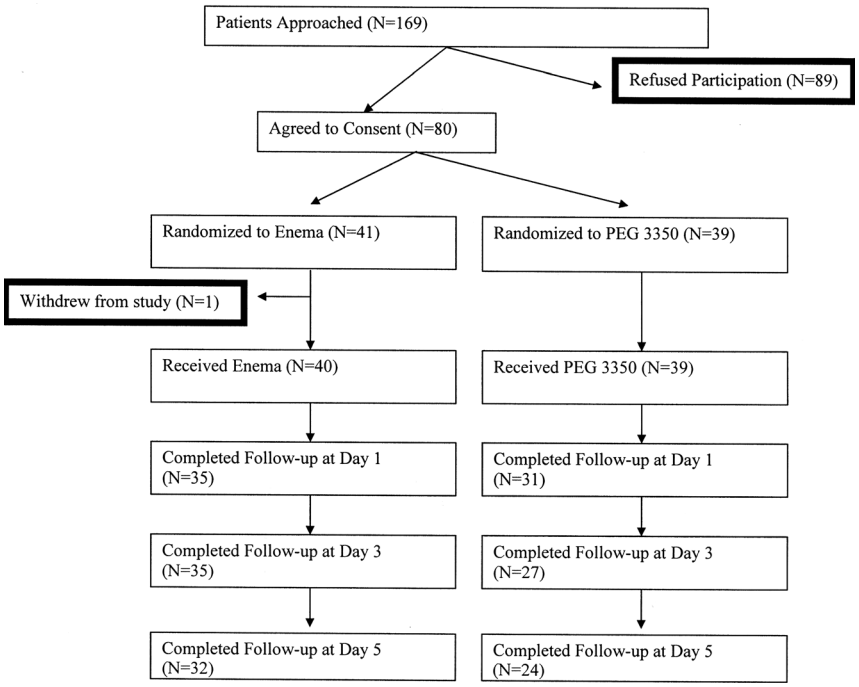

FIGURE 1. Study flowchart.

however, those who refused were significantly older (8.4 vs 6.9 years; $P < 0.05$).

Participant characteristics are noted in Table 1. There were no significant differences between the treatment arms in subject age, sex, race/ethnicity, or constipation history in previous 3 months. Most subjects (82%) reported their main symptom as "abdominal/side pain" or "constipation" with no variation between treatment arms. Vomiting (4%), GU complaints (3%), other GI complaints (4%), and other complaints (6%) were also reported as main symptoms.

A total of 56 (71%) subjects completed the 5-day follow-up with more patients completing follow-up in enema arm but the difference was not statistically significant (80% vs 62%; $P = 0.07$). At day 3, significantly more subjects in the oral cleanout arm were lost to follow-up than the enema arm (31% vs 13%;

TABLE 1. Participant Characteristics

	Total (N = 79)	PEG Arm (n = 39)	Enema Arm (n = 40)
Mean age, y	6.9 ± 0.5	6.9 ± 0.7	6.8 ± 0.7
Age group, y, n (%)			
1–4	30 (38)	15 (38)	15 (37)
5–9	31 (39)	15 (38)	16 (40)
11–17	18 (23)	9 (23)	9 (23)
Female, n (%)	46 (58)	20 (51)	26 (65)
Ethnicity/race, n (%)			
African American	31 (39)	14 (36)	17 (43)
White	30 (38)	18 (46)	12 (31)
Hispanic/Latino	11 (14)	5 (13)	6 (15)
Other/missing	7 (9)	2 (5)	5 (12)
Constipation history, n (%)			
Ideal stool consistency*	38 (48)	21 (54)	17 (43)
Infrequent stools[#]	30 (38)	12 (31)	18 (45)
Main symptom, n (%)			
Abdominal pain	34 (43)	18 (46)	13 (33)
Constipation	31 (39)	13 (33)	21 (53)

*"Not too hard and not too soft" or "very soft and mushy."

[#]Less than 2 stool passages per week.

TABLE 2. Intervention Analysis

	n (%)		OR
	PEG	Enema	(95% CI)
Day 1			
Ideal stool consistency	11 (48)	11 (61)	0.6 (0.2–2.0)
Strain with BM	3 (14)	6 (33)	0.3 (0.7–1.6)
Improvement in main symptom	16 (55)	28 (82)	0.3 (0.1–0.8)
Day 3			
Ideal stool consistency	15 (60)	29 (94)	0.1 (0.0–0.5)
Strain with BM	7 (28)	6 (20)	1.6 (0.5–5.6)
Improvement in main symptom	23 (89)	30 (91)	0.8 (0.1–4.2)
Regular BM pattern	9 (45)	20 (65)	0.5 (0.1–1.4)
Day 5			
Ideal stool consistency	17 (71)	26 (90)	0.3 (0.6–1.2)
Strain with BM	5 (21)	6 (20)	1.1 (0.3–4.0)
Improvement in main symptom	22 (92)	28 (93)	0.8 (0.1–6.0)
Regular BM pattern	12 (67)	22 (79)	0.5 (0.1–2.1)

Analysis of intervention (enema vs oral PEG arm) on specific outcomes; ORs with 95% CIs are described. Subjects for whom follow-up data were not available or who answered "don't know" were omitted from analysis.

BM indicates bowel movement.

$P < 0.05$). There was no difference in lost patients by age group at any follow-up. Treatment failures occurred in 6 patients.

Follow-Up Day 1

Patients in the oral cleanout arm were less likely to have improvement in their main symptom (OR, 0.3; 95% CI, 0.1–0.8; Table 2). There was no difference between the groups in straining or stool consistency.

The mean number of stools was higher in the oral cleanout arm (2.2 vs 1.0; $P < 0.05$; Fig. 2) and significantly more patients reported no stools since ED discharge in the enema arm (49% vs 28%; $P = 0.05$). One patient in the enema arm reported using a treatment (dietary changes) that was not prescribed at the ED visit.

The majority (54%) of children in the enema arm were reported as "somewhat upset" or "very upset" by the therapy, whereas no children in the oral cleanout arm were upset ($P < 0.05$). The majority of all families (95%) reported their ED visit was "very helpful."

Follow-Up Day 3

There were no differences between the treatment groups in improvement of main symptom or straining at day 3. More patients in the enema arm reported an ideal stool consistency (74% vs 38%; $P < 0.05$). The mean number of stools was higher in the oral cleanout arm (4.2 vs 2.7; $P < 0.05$). About half (48%) of all patients were having their regular pattern of bowel movements, and there was no difference between treatment groups. Use of a treatment that was not prescribed at the ED visit was noted only for treatment failures.

Follow-Up Day 5

There were no differences between the treatment groups in improvement of their main symptom, straining, number of stools, or stool consistency at day 5. The majority (61%) of all patients reported a regular pattern of bowel movements with no difference between treatment groups.

With the exception of subjects failing treatment (Table 3), none reported using a treatment that was not prescribed at the ED visit. Most (98%) had started their maintenance dose of PEG 3350 with no difference between the groups.

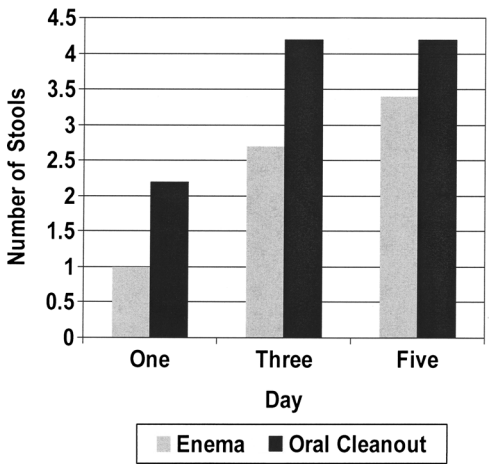

FIGURE 2. Stool frequency—Subjects provided number of stools since last contact. The mean number of stools was higher in the oral cleanout arm at all points, which was significant on days 1 and 3 ($P < 0.05$).

TABLE 3. Treatment Failures

Arm	Age, y	Outcome
PEG	10.3	ED return and admit for oral cleanout for constipation
PEG	10.3	Home enema, later ED return and admit for oral cleanout for constipation
PEG	9.3	Home enema
		Some improvement after enema, follow-up PCP
PEG	3.1	ED return
		Diagnosed with UTI and constipation, treated with Keflex and PEG 3350
Enema	2.8	ED return
		Diagnosed with viral infection causing fever and vomiting (urinalysis normal), treated with supportive care
PEG	2.8	ED return
		Diagnosed with constipation, treated with continued PEG 3350

PCP indicates primary care physician.

Treatment Failures

Table 3 describes treatment failures. Of the 6 subjects who were failures, 5 were in the oral cleanout arm, which neared statistical significance ($P = 0.08$). Two received an enema at home, 5 returned to the ED, and 2 were subsequently admitted to an inpatient unit for disimpaction.

DISCUSSION

To the best of our knowledge, this study is among the first randomized trials to compare enema to oral PEG for fecal impaction in children. Our results indicate that an enema may relieve symptoms faster than oral PEG in pediatric patients with fecal impaction; however, the greater improvement of symptoms in the enema arm, likely the result of immediate passing of stool, was not sustained beyond day 1. Because the onset of action for PEG 3350, when used in this form, is approximately 2 days,[25] most subjects in both arms have increased stool frequency and experiencing potential benefits of disimpaction by days 3 and 5.

Stool frequency is an objective measure frequently used when evaluating constipation treatments, and one goal of therapy is to increase stool frequency. In our study, subjects in the oral cleanout arm had increased stool frequency at each follow-up point, but experienced delayed symptom improvement. Although the number of stools was higher in the oral cleanout arm at all points, subjects in the enema achieved ideal stool consistency sooner. This may indicate that enema subjects were disimpacted sooner, whereas subjects in the oral cleanout arm continued to have frequent stools that were either too hard or too runny.

Since the initiation of this study, several additional studies evaluating the efficacy of PEG-based laxatives have been published: most compared PEG to another oral agent. In a recent systematic review, Pijpers et al[20] reported that PEG-based treatments have been proven as or more effective than placebo, lactulose, or milk of magnesia for constipated children.

Bekkali et al,[19] in a single randomized trial addressing treatment of fecal impaction, reported enema and PEG to be equally effective. This study differed from ours in several ways: treatment was longer (6 vs 3 days) and disimpaction was determined by repeat digital rectal examination or abdominal radiograph, whereas we focused on symptom improvement. Interestingly,

the authors reported more treatment failures in the PEG arm, similar to our study.

By comparing 2 treatment options for symptom relief caused by fecal impaction, our study helps to fill a gap in the literature. In this study, enemas produced more rapid initial symptom improvement and less-frequent stools but resulted in a significant number of upset subjects. Oral PEG produced slower improvement in initial symptoms and more frequent stools but did not cause significant subject upset with treatment. Knowledge of these results has the potential to assist patients, families and health care providers in making informed decisions about treatment options.

Despite treatment arm and subject outcome, almost all caregivers (95%) reported their ED visit was "very helpful." Perhaps families responded well to the education from researchers about constipation, which often is a long-term problem.

LIMITATIONS

One limitation of this study is potential selection bias. More than half of patients who were approached declined participation. Many patients or caregivers had a preferred treatment in mind and the most common reason why eligible patients refused to participate was refusal to be randomized. Teenagers were particularly difficult to enroll. It is unknown what treatment response these refusals may have had. Additionally, blinding was not possible in this study and this may have affected interpretation of effects from the intervention. Also, although our study was limited by a small number of participants, this number is similar to or greater than other pediatric constipation studies.[10,11,13,15,17,18,21] Finally, a moderate number of patients (29%) were lost to follow-up by day 5, which is comparable to other studies conducted in this setting. Because it is unknown what final treatment response was obtained in these subjects, there were no significant differences between treatment arms, and the proportion lost from each arm was similar, we analyzed our data without including these subjects. [26]

CONCLUSIONS

This pilot study suggests that disimpaction by enema may be superior to PEG for more immediate relief of symptoms in the acute care setting. Symptoms and signs of treatment effect did not differ beyond 24 hours. When considering treatment, this initial benefit needs to be balanced with the potential distress that may be associated with enemas. Larger trials will be needed to assess any advantage.

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