Digestive Diseases and Sciences, Vol. 41, No. 8 (August 1996), pp. 1636–1642

Small Volume Isosmotic Polyethylene Glycol Electrolyte Balanced Solution (PMF-100) in Treatment of Chronic Nonorganic Constipation

E. CORAZZIARI, MD, D. BADIALI, MD, F.I. HABIB, MD, G. REBOA, MD, G. PITTO, MD, G. MAZZACCA, MD, F. SABBATINI, MD, R. GALEAZZI, MD, Te. CILLUFFO, MD, I. VANTINI, MD, E. BARDELLI, MD, and F. BALDI, MD

The present multicenter double-blind placebo-controlled trial evaluates the therapeutic effectiveness of small-volume daily doses of an isosmotic polyethylene glycol (PEG) electrolyte solution in the treatment of chronic nonorganic constipation. After a complete diagnostic investigation, patients still constipated at the end of a four-week placebo-treatment run-in period were enrolled and randomized to receive either placebo or PEG solution 250 ml twice a day for the following eight weeks. Patients were assessed at four and eight weeks of treatment, and they reported frequency and modality of evacuation, use of laxatives, and relevant symptoms daily on a diary card. Oroanal and segmental large-bowel transit times were assessed with radiopaque markers during the fourth week of the run-in period and the last week of the treatment period. During the study period, dietary fiber and liquids were standardized and laxatives were allowed only after five consecutive days without a bowel movement. Of the 55 patients enrolled, five dropped out, three because of adverse events and two for reasons unrelated to therapy; another two were excluded from the efficacy analysis because of protocol violation. Of the remaining 48 patients (37 women, age 42 ± 15 years, mean ± SD), 23 were assigned to placebo and 25 to PEG treatment. In comparison to placebo, PEG solution induced a statistically significant increase in weekly bowel frequency at four weeks and at the end of the study (PEG: 4.8 ± 2.3 vs placebo: 2.8 ± 1.6; $P < 0.002$) and a significant decrease in straining at defecation ($P < 0.01$), stool consistency ($P < 0.02$), and use of laxatives ($P < 0.03$). Oroanal, left colon, and rectal transit times were significantly shortened by PEG treatment. There was no difference between controls and PEG-treated patients as far as abdominal symptoms and side effects were concerned. In conclusion, PEG solution at 250 ml twice a day is effective in increasing bowel frequency, accelerating colorectal transit times, and improving difficult evacuation in patients with chronic nonorganic constipation and is devoid of significant side effects.

KEY WORDS: constipation; polyethylene glycol; transit times.

Adequate diet and fiber intake, which are the first therapeutic measures in chronic constipation, appear to be generally inadequate since, in spite of their prescription, the use of laxatives is reported by 88% of patients with chronic constipation and laxative consumption increases with age and duration of constipation (1). However, even the usual laxatives are far from satisfactory as, in about 30% of constipated

Manuscript received November 21, 1995; revised manuscript received March 25, 1996; accepted May 23, 1996.

From the Cattedra di Gastroenterologia I, Universitá La Sapienza, Rome; Clinica Chirurgica, Universitá degli Studi, Genoa; Cattedra di Gastroenterologia, II Facoltà di Medicina, Policlinico II, Naples; Divisione di Gastroenterologia, Ospedale Regionale Umberto I, Ancona; Divisione di Riabilitazione Gastroenterologica, Facoltà di Medicina, Universitá degli Studi Verona, Ospedale Valeggio S/M; and Divisione di Gastroenterologia, Policlinico S. Orsola, Bologna, Italy.

Address for reprint requests: Dr. Enrico Corazziari, Cattedra di Gastroenterologia I, Clinica Medica II, Policlinico "Umberto I," 00161 Rome, Italy.

0163-2116/96/0800-1636$09.50/0

patients, they fail to normalize bowel frequency, do not ameliorate the constipation-associated symptoms of flatulence, abdominal pain, and bloating and, when abused, cause several side effects due to dehydration and/or electrolyte depletion (1–3).

Experience with orthograde whole-gut irrigation in preparing for colon investigation and surgery (4) initially using an electrolyte solution and later an isosmotic polyethylene glycol electrolyte solution (PEG) has led to its use in the acute treatment of both fecal impaction (5, 6) and severe constipation (7, 8). Results have been favorable, and plasma volume and electrolyte balance have not been affected. To perform whole-gut irrigation and treat acute constipation, the recommended dose is one gallon of PEG solution taken orally over 120–150 min. However, more recently, two randomized controlled trials have shown that low daily doses (8–16 oz) of isosmotic PEG can be effective in the acute (five to eight days) treatment of chronic constipation (9, 10).

The aim of the present trial was to assess the therapeutic effectiveness of low daily doses of isosmotic PEG in the treatment of chronic nonorganic constipation over a two-month period. Simethicone was added to the PEG preparation (PMF-100 Promefarm Srl, Milan, Italy) with the intent to alleviate the abdominal symptoms usually associated with constipation.

MATERIALS AND METHODS

Patients. Patients seeking medical advice for chronic constipation were investigated in the outpatient clinics of the centers participating over the period from January 1993 to May 1994.

To meet the inclusion criteria, patients had to be 18–70 years old and have chronic constipation defined as follows (2): less than two bowel movements (BM) per week, for at least 12 months, or presence of two or more of the following complaints (when laxatives and/or enema were not used): less than three BM per week; straining at defecation; sense of incomplete evacuation and hard stools on at least 25% of occasions.

Constipation, as defined above, still had to be present at the end of the run-in period (see study design). Other criteria were negative tests for organic disorders of the digestive tract, no anorectal lesions, no abnormality at barium enema or colonoscopy, and normal laboratory tests (routine laboratory examinations plus serum calcium, phosphate, T3, T4, and TSH).

Exclusion criteria were: inflammatory bowel disease; patients not meeting inclusion criteria; pregnant women or women not using effective contraceptive measures; previous surgery on the gastrointestinal tract, except appendectomy and cholecystectomy; chronic use of drugs affecting gastrointestinal motility; chronic systemic metabolic, neurological, and psychiatric illnesses. The protocol was approved by the Ethical Committee of the II Clinica Medica, Università "La Sapienza," Rome. All subjects gave their written informed consent.

Study Design. This was a multicenter (six centers) trial run according to a randomized double-blind, placebo-controlled, parallel group design. The study protocol included a four-week run-in period and one eight-week active treatment period (divided into two four-week periods), for a total of three four-week observation periods. After medical history and physical examination at visit 1, patients entered the run-in period, during which they took placebo and were instructed to standardize their diet so as to have a mean daily intake of 15 g of fiber and 1500 ml of water and to refrain from laxatives and enemas. The patients who met the inclusion criteria at the end of the run-in period were enrolled in the study (visit 2) and were allocated to receive, in a double-blind fashion for the following eight weeks, either placebo or active treatment according to a randomization code that was independent for each center.

During the run-in and study periods, no other medication was allowed. Laxatives were allowed only when patients had no bowel movements for at least five consecutive days. After four weeks of treatment and again at the end of the study, patients were required to attend for a visit (visits 3 and 4).

At each of the four visits, patients underwent physical examination and were interviewed, using a standardized questionnaire, in order to assess the occurrence and severity of symptoms and the acceptability of the preparations. The modality of evacuation as well as the following relevant symptoms were assessed: abdominal pain, abdominal bloating, flatulence, borborygmi, anorexia, headache, asthenia, nausea.

At visits 1, 2, and 3 patients were given 60 sachets for the subsequent four-week treatment period and four weekly diary cards on which they reported daily the number of sachets taken, number of evacuations, stool consistency (soft, firm, hard, pellety), straining (absent, slight, marked) at defecation, use of laxatives, and relevant symptoms. At visits 2, 3, and 4 patients returned the completed diary cards and the remaining sachets.

Gastrointestinal Transit Time (GITT). In four centers, total and segmental large-bowel transit was assessed in series of four patients assigned to an *ad hoc* randomization block consisting of two placebo and two PMF-100 treatments. Large-bowel transit was assessed during the fourth week of the run-in period and the eighth week of the treatment period. Three doses of differently shaped (ring, disk, and cylinder) radiopaque markers (Department of Internal Medicine, Kantonsspital, Basle; P. & A. Mauch, Münchenstein; Janssen Pharmaceutica AG, Basle; Switzerland) were used to assess total and segmental large bowel transit times. Each dose of 20 markers was ingested during breakfast on three consecutive days. The number and location of the differently shaped markers were assessed on an abdominal x-ray performed 24 hr after ingestion of the third dose.

Twenty patients were enrolled; 11 (all women; age: 41.7 ± 18 years) were allocated to receive placebo and nine (six women, three men; age: 34 ± 14 years) to receive PMF-100. One patient of the placebo groups did not un-

TABLE 1. PATIENT POPULATION PROFILE AT END OF RUN-IN PERIOD

	Placebo group		*PMF-100 group*	
	Entire group (N = 23)	*Transit assessed (N = 10)*	*Entire group (N = 25)*	*Transit assessed (N = 9)*
Sex F/M	20/3[a]*	10/0[b]	17/8[a]	6/3[b]
Age (yr)	43.5 ± 15.1†	41 ± 18†	40.3 ± 14.4†	34 ± 14†
Duration of constipation (yr)	15.7 ± 13.3†	14.5 ± 8.8†	10 ± 8.8†	14.41 ± 10.3†
Bowel frequency (per week)	1.9 ± 0.8†	2.1 ± 0.8†	2.2 ± 0.5†	2.2 ± 0.5†
Straining at defecation				
Slight	12[a]	7[a]	14[a]	8[a]
Marked	11	3	11	1
Use of laxative	13	4	16	5
Stool consistency				
Soft	0	0	4	4
Firm	8	7	6	3
Hard/pellety	15	3	14	2

* Differences between treatments: [a], χ^2 test = NS; [b], Fisher exact test = NS.
† Mean ± SD, Student's t test = NS.

dergo the second assessment as she did not complete the study because of an intervening adverse event.

Treatment. Active treatment, PMF-100, was supplied as a granular preparation contained in sachets. Each 17.5g- sachet contained the following active ingredients: polyethylene glycol 4000, 14.6 g; anhydrous sodium sulfate, 1.42 g; sodium bicarbonate, 0.42 g; sodium chloride, 0.36 g; potassium chloride, 0.18 g; and simethicone (activated dimethicone), 0.01 g. Placebo, containing 16.92 g of orange-flavored maltdextrine, was supplied in identical form and the smell, color, and taste of both preparations was the same. Patients were instructed to dissolve the contents of each sachet in 250 ml of water before ingestion. The dosage was one sachet twice daily; patients were allowed to reduce the dosage to once daily, according to BM. In no case were they allowed to increase the dosage.

Patient Assessment. Bowel frequency, straining at defecation, stool consistency, use of laxatives and relevant symptoms were collected from data reported on the diary card and assessed at each visit. Bowel frequency was expressed as the number of evacuations per week, over the three four-week study periods, and normal frequency was considered to be at least three evacuations per week.

The severity of each symptom was scored by the physician on a four-point scale: absence of symptoms (0) and mild (1), moderate (2), and severe (3) symptoms. The score for each symptom was evaluated separately.

Compliance with treatment was assessed by direct interview of the patients, checking the diary cards where the daily number of sachets taken was recorded and counting the sachets brought back by the patient at the end of each four-week study period. Oroanal transit time was expressed as the time interval between the ingestion and the evacuation of at least 80% of the first dose of markers. Total and segmental transit through the large bowel were expressed as the mean daily percentages of markers excreted from the entire large bowel and also the right colon, left colon, and rectum, at the 72nd hour (transit index) (11).

Statistical Analysis. To assess the therapeutic effectiveness of PMF-100, the primary criteria were bowel frequency and normalization of bowel frequency; the secondary criteria were use of laxatives, straining at defecation, stool consistency, and other symptoms.

The power of the trial, based on 2.5 BM/week for placebo and 4.5 BM/week for active treatment with a standard deviation of 2.3, and 21 patients per group, was higher than 0.8 for a two-tail test at 0.05 level.

Results are expressed as mean and standard deviation. The chi-square test was used for the analysis of straining at stool, use of laxatives, stool consistency, bowel normalization, and symptoms.

Analysis of variance (ANOVA) was used to assess bowel frequency. Results were assessed per protocol and, when compatible, per intention to treat analysis.

RESULTS

The six centers participating enrolled 55 patients, five of whom failed to complete the study, one because of protocol violation (dosage), one lost to follow-up, and three because of adverse events: one (placebo) had an allergic reaction, one (PMF-100) had abdominal pain, and one (placebo) had uroseptic fever requiring hospitalization.

Of the remaining 50 patients who completed the study, two were excluded from the efficacy analysis: one because of continuous use of cathartics and one because the inclusion criteria were not met (seven BM weekly at the end of the run-in period). The 48 patients who completed the study in a satisfactory manner consisted of 11 men and 37 women (mean age ± SD: 41.8 ± 14.8 years; range 18–70); 23 patients were assigned to placebo treatment (group I) and 25 to PMF-100 treatment (group II). The patient profiles are summarized in Table 1. The two groups were comparable in sex, age, and baseline features of constipation.

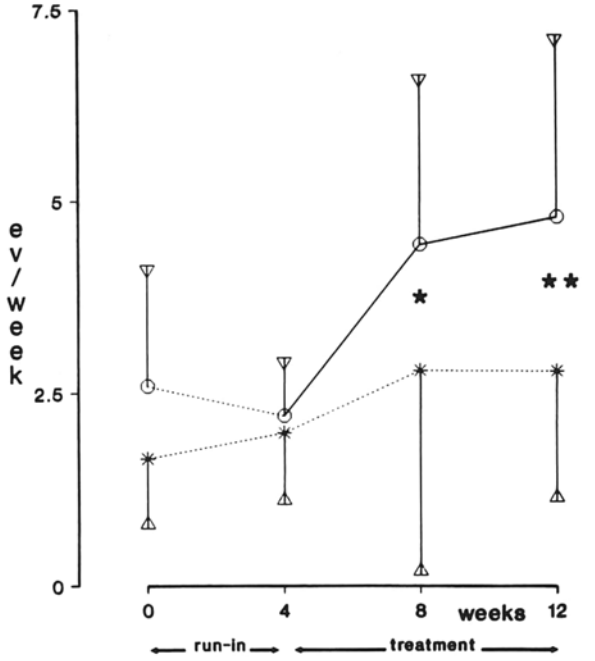

Fig 1. Weekly bowel frequency (mean ± SD) during run-in period and treatment period. Evacuations per week increased significantly during PMF-100 administration (solid line) in comparison to placebo (dotted line) after 8 (* $P < 0.05$) and 12 weeks (** $P < 0.002$) of treatment.

The two groups showed no significant difference in stool frequency, straining at defecation, stool consistency, and use of laxatives at the end of the run-in period (Table 1). Mean daily sachet intake did not differ between the placebo group ($N = 17$; mean ± SD 1.7 ± 1.7 sachets daily) and the PMF-100 group ($N = 18$; mean ± SD 1.6 ± 0.5 sachets daily). PMF-100 induced a statistically significant ($P < 0.002$) increase in the number of BM at the fourth and the eighth week of treatment (Figure 1). At the end of the treatment period, the weekly bowel frequency averaged 4.8 ± 2.3 in PMF-100 treated patients (run-in bowel frequency: 2.2 ± 0.5 BM/week) and 2.8 ± 1.6 in patients receiving placebo (run-in bowel frequency: 1.9 ± 0.8 BM/week). Bowel frequency was normalized in 64% of the patients on PMF-100 treatment compared to 22% of those on placebo ($P < 0.008$; per intent-to-treat analysis $P < 0.04$ vs placebo). Straining at defecation decreased ($P < 0.01$ vs placebo) during PMF-100 treatment (Figure 2) (per intent-to-treat analysis $P < 0.1$ vs placebo).

On completion of treatment, marked straining was still reported by 41% of the placebo-treated patients and by 8% of those receiving active treatment ($P < 0.03$).

Stool consistency was reduced ($P < 0.02$ vs placebo) at the end of PMF-100 administration. At the end of treatment, 50% of the placebo-treated patients complained of hard/pellety stool versus 12% of the PMF-100 group (Figure 3, per intent-to-treat analysis $P < 0.07$ vs placebo). PMF-100 treatment significantly reduced ($P < 0.03$ vs placebo) the use of laxatives, which occurred in 16% of the active treatment group and in 48% of the placebo-treated group (per intent-to-treat $P < 0.1$ vs placebo).

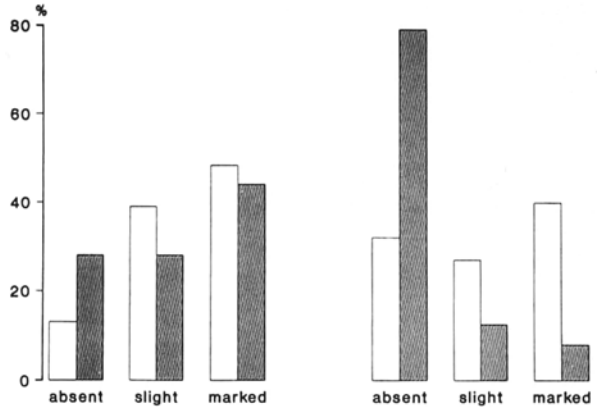

Fig 2. Percentage of patients straining at defecation during run-in period (left) and treatment period (right). During treatment a significant difference ($P < 0.01$) was observed between placebo (empty columns) and PMF-100 (filled columns) group.

All patients considered the solution easy to administer; 79% judged the amount taken to be proper, whereas 19% found it excessive. The taste of PMF-100 was considered good, indifferent, and tolerable by 20%, 44%, and 36% of the patients, respectively. The taste of placebo was considered good, indifferent, and

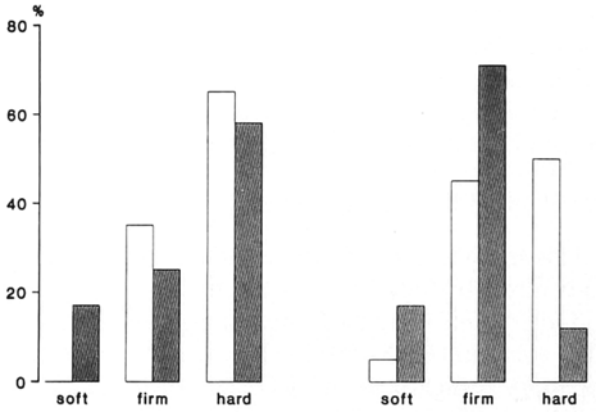

Fig 3. Stool consistency referred by patients (percentage) during run-in (left) and treatment period (right). Stool consistency decreased significantly ($P < 0.02$) during PMF-100 treatment in comparison to placebo treatment. Empty columns indicate placebo-treated patients. Filled columns indicate PMF-100-treated patients.

TABLE 2. RELATIVE OCCURRENCE (%) OF SYMPTOMS DURING STUDY PERIOD

	Run-in		*Treatment period*	
Symptoms	*Placebo (%)*	*PMF-100 (%)*	*Placebo (%)*	*PMF-100 (%)*
Abdominal pain	52	60	35	24
Abdominal bloating	91	84	70	48
Flatulence	48	29	39	20
Borborygmi	26	24	13	32
Anorexia	13	8	13	4
Headache	9	21	13	4
Asthenia	9	4	4	4

tolerable by 17%, 61%, and 22% of patients, respectively; no significant difference in taste was found between the two solutions.

GITT. The patients who underwent large bowel transit assessment did not differ from the other patients enrolled in age, sex, and relevant clinical characteristics of constipation (Table 1). Oroanal transit time measured at the end of the run-in period was at least 96 hours in all the patients investigated. The transit of markers through the large bowel accelerated significantly during PMF-100 treatment (TI: 19 ± 25 run-in period vs 39 ± 21 PMF-100; $P < 0.05$) and did not vary during placebo treatment (TI: 14 ± 17 run-in period vs 26 ± 20 placebo, NS). During PMF-100 treatment, the transit of markers did not vary through the right colon (TI: 67 ± 27 run-in period vs 74 ± 10, NS), and it was significantly accelerated through the left colon (TI: 46 ± 29 run-in period vs 62 ± 20, $P < 0.05$) and the rectum (TI: 37 ± 42 run-in period vs 78 ± 21, $P < 0.05$).

Symptoms and Side Effects. Symptoms reported at the beginning and end of treatment are set out in Table 2. The occurrence of the symptoms investigated did not differ significantly between the two treatment groups. Symptom severity showed no difference between placebo and PMF-100-treated patients.

DISCUSSION

This multicenter randomized, double-blind placebo-controlled study assessed the therapeutic efficacy and tolerability of a new formulation of an electrolyte PEG solution (PMF-100) in chronic nonorganic constipation. A high dose of PEG electrolyte solution is widely used for bowel cleansing before intestinal surgery and radiological and endoscopic large bowel preparation. The usual doses range from 2 to 4 liters, and its cleansing efficacy and its tolerability have been well established (12).

PEG–electrolyte solutions (ELS-PEG, Golytely, SELG) have been used with favorable results in the treatment of chronic constipation, initially at a high dose in a single administration (13) and subsequently at low daily doses (9, 10). In the two previous double-blind placebo-controlled studies, by Andorsky and Goldner (9) and by Baldonedo et al (10), a low daily dose of PEG solution caused a significant improvement in mean stool frequency and consistency. However, these two studies offer only limited information on the possible therapeutic role of PEG–electrolyte solution in chronic constipation since: (1) the observation period was limited to five days in one and eight days in the other; (2) the definition of constipation was based on patients' reports and the patients investigated averaged 4–5 BM/week on placebo treatment; (3) the treatment was not preceded by a run-in period; and (4) the crossover design did not include a washout period between the two treatments.

More recently in a controlled study in which blindness could not be achieved, Klauser et al. (14) reported improvement of chronic slow transit constipation with low daily doses of electrolyte free PEG solutions, which can induce, however, marked loss of plasma ions (15).

In the present study, daily low doses of isosmotic and electrolyte-balanced PEG solution were administered for a period of eight weeks in patients who complied with an international standardized objective definition of chronic constipation even after a four-week run-in period of placebo administration. The multicenter structure of the trial prevented patients from being submitted to extensive standardized investigation to assess the underlying role of slow transit and/or pelvic floor disorders in each individual patient. Nonetheless, the strict entry criteria are a guarantee that the population selected was homogeneous for the presence of genuine and persistent bowel alterations. This placebo-controlled trial showed that the administration of PMF-100 increased weekly bowel frequency and reduced straining at defecation, stool consistency, and the use of laxatives throughout the eight-week study period with the mean daily dose of 400 ml solution.

These results are similar to those obtained by Andorsky and Goldner, who suggested that the daily dosage should be between 8 and 16 oz, corresponding to 223 and 446 g of solution. The assessment of the total and segmental large bowel transit was performed in a subgroup of patients who did not differ from the entire group of enrolled subjects from whom they were randomly selected. The administration of

PMF-100 increased the excretion of markers from the large bowel by accelerating the transit of contents through the left colon and the rectum, whereas no significant effect on transit through the right colon could be detected. The lack of variation in the right colon transit time does not necessarily demonstrate that PMF-100 has no effect on the right colon. It may simply reflect the inability of the radiologic technique to detect transit time variations of less than 24 hr, as this might be the case for right colon transit, which was normal in basal conditions in most of the patients. No specific untoward side effects were reported during PMF-100 treatment; in one patient the active treatment was discontinued because of abdominal pain, but this symptom should not be regarded as a specific PMF-100 side effect as it was present to an equal degree in the placebo and active-therapy patient groups.

The administration of PMF-100 was not accompanied by symptoms such as abdominal cramps, diarrhea, and urgent defecation, which may follow the administration of stimulant laxatives. Bloating and flatulence, which are frequent side effects of bulking agents and laxatives undergoing bacterial degradation, occurred in only a relatively small proportion of patients. The symptoms investigated did not vary significantly, confirming a poor relationship between abdominal symptoms and bowel frequency (16). Patients' acceptance of the solution was satisfactory, as regards both taste and volume of fluid intake.

CONCLUSIONS

The present data show that PMF-100 at low daily doses may be of benefit in the treatment of chronic constipation, at least for a two-month period. The demonstration of its therapeutic efficacy without significant side effects makes PMF-100 at low daily doses an alternative to other laxatives. PEG is in fact an inert, nontoxic (17) polymer that is not degraded by bacteria, is scarcely absorbed by normal (<0.06%) and inflamed (<0.09%) mucosa (18) and is rapidly excreted by the kidney (19). In addition, even when large volumes are administered, PEG–electrolyte solutions do not affect water and electrolyte balance (4, 19) and cause less damage to the colon mucosal epithelia than osmotic and stimulant laxatives (20).

Although it is likely that the specific properties of PEG–electrolyte solution make it suitable for chronic use, the lack of properly scheduled biochemical analysis in the present trial does not allow low daily doses of PMF-100 to be advocated in the long-term treatment of chronic constipation, which should be assessed in properly designed studies. Likewise, the cost–benefit ratio of PEG–electrolyte solution in comparison to other treatments for chronic constipation should be properly assessed.

ACKNOWLEDGMENTS

We are grateful to Ms. J. Gribble for revision of the English language.

REFERENCES

1. Corazziari E, Materia E, Bausano G, Torsoli A, Badiali D, Fanucci A, Fraracci L, Morini S, Capurso L, Montesi A, Pinzello G, Novara V: Laxative consumption in chronic nonorganic constipation. J Clin Gastroenterol 9:427–430, 1987
2. Whitehead WE, Chaussade S, Corazziari E, Kumar D: Report of an international workshop on management of constipation. Gastroenterol Int 4:99–113, 1991
3. Clayden GS: Management of chronic constipation. Arch Dis Child 6:340–344, 1992
4. Davis GR, Santa Ana CA, Morawski SG, Fordtran JS: Development of a lavage solution associated with a minimal water and electrolyte absorption or secretion. Gastroenterology 78:991–995, 1980
5. Ingebo KB, Hayman MB: Polyethylene glycol–electrolyte solution for intestinal clearance in children with refractory encopresis. Am J Dis Child 3:340–342, 1988
6. Tolia V, Lin CH, Elitsur Y: A prospective randomized study with mineral oil and oral lavage solution for treatment of fecal impaction in children. Aliment Pharmacol Ther 7:523–529, 1993
7. Smith RG, Currie JJ: Whole gut irrigation: A new treatment for constipation. BMJ 8:396–397, 1978
8. Millar AJW, Rode H, Buchler J, Gywes S: Whole-gut lavage in children using an iso-osmolar solution containing polyethylene glycol (Golytely). J Pediatr Surg 9:822–824, 1988
9. Andorsky RI, Goldner F: Colonic lavage solution (polyethylene glycol electrolyte lavage solution) as a treatment for chronic constipation: A double-blind, placebo-controlled study. Am J Gastroenterol 85:261–265, 1990
10. Baldonedo YC, Lugo E, Uzcategui AA, Guelrud M, Skornicki J: Evaluacion y uso del polietilen glicol en pacientes constipados. Gen (Venezuela) 45:294–297, 1991
11. Corazziari E, Dani S, Possessere C, Anzini F, Torsoli A. Colonic segmental transit times in non-organic constipation. Rend Gastroenterol 7:67–69, 1975
12. Ernstoff J, Howard DGA, Marshall JB, Jumshyd A, McCullough AJ: A randomized blinded clinical trial of a rapid colonic lavage solution (Golytely) compared with standard preparation for colonoscopy and barium enema. Gastroenterology 84:1512–16, 1983
13. Saggioro A: Trattamento della stipsi in ambito geriatrico con una soluzione di lavaggio gastrointestinale. Risultati di uno studio controllato. Il Gastroenterologo 6:19–21, 1992
14. Klauser AG, Muhldorfer BE, Voderhlzer WA, Wenzel G, Muller-Lissner SA: Polyethylene glycol 4000 for slow transit constipation. Z Gastroenterol 33:5–8, 1995
15. Fordtran JS, Santa Ana CA, Cleveland MvB: A low sodium

solution for gastrointestinal lavage. Gastroenterology 98:11–16, 1990
16. Badiali D, Corazziari E, Habib FI Tomei E, Bausano G, Magrini P, Anzini F, Torsoli A: The effect of wheat bran in the treatment of chronic nonorganic constipation. A double-blind controlled trial. Dig Dis Sci 40:349–356, 1995
17. Chadwick VS, Phillips SF, Hofmann AF: Measurements of intestinal permeability using low molecular weight polyethylene glycols (PEG 400). Gastroenterology 73:241–246, 1977
18. Brady CE, Di Palma JA, Morawski SG, Santa Ana CA, Fordtran JS: Urinary excretion of polythylene glycol 3350 and sulfate after gut lavage with a polythylene glycol electrolyte lavage solution. Gastroenterology 90:1914–1918, 1986
19. Di Piro JT, Michael KA, Clark BA, Dickson P, Vallner JJ, Dower TA, Tedesco FJ: Absorption of polythylene glycol after administration of a PEG electrolyte lavage solution. Clin Pharmacol 5:153–155, 1986
20. Philip J, Schubert GE, Thiel A, Wolters U: Preparation for colonoscopy using Golytely, a sure method? Comparative histological and clinical study between lavage and saline laxative. Med Klin 85:415–420, 1990