Safety of Polyethylene Glycol 3350 for the Treatment of Chronic Constipation in Children

Dinesh S. Pashankar, MD, MRCP; Vera Loening-Baucke, MD; Warren P. Bishop, MD

Objectives: To assess the clinical and biochemical safety profile of long-term polyethylene glycol 3350 (PEG) therapy in children with chronic constipation and to assess pediatric patient acceptance of PEG therapy.

Design: Prospective observational study.

Setting: Pediatric clinics at a referral center.

Patients: Eighty-three children (44 with chronic constipation, 39 with constipation and encopresis) receiving PEG therapy for more than 3 months.

Main Outcome Measures: Clinical adverse effects related to PEG therapy and acceptance and compliance with PEG therapy. Serum electrolyte levels, osmolality, albumin levels, and liver and renal function test results were measured.

Results: At the time of evaluation, the mean duration of PEG therapy was 8.7 months, and the mean PEG dose was 0.75 g/kg daily. There were no major clinical adverse effects. All blood test results were normal, except for transient minimal alanine aminotransferase elevation unrelated to therapy in 9 patients. All children preferred PEG to previously used laxatives, and daily compliance was measured as good in 90% of children.

Conclusions: Long-term PEG therapy is safe and is well accepted by children with chronic constipation with and without encopresis.

Arch Pediatr Adolesc Med. 2003;157:661-664

Common problem in the pediatric population. This symptom accounts for 3% of outpatient visits to general pediatric clinics and up to 25% of visits to pediatric gastroenterology clinics. Treatment regimens vary widely and include dietary and behavioral modification, counseling, and the use of various laxatives and stool softeners.

Polyethylene glycol 3350 (PEG) is a relatively new osmotic laxative. Polyethylene glycol is a component of the PEG-electrolyte lavage solution that has been used in large volume to cleanse the gastrointestinal tract for diagnostic and surgical procedures in children. Polyethylene glycol 3350 is a nontoxic and highly soluble compound that is minimally absorbed in the gastrointestinal tract. Due to these properties, PEG acts as an osmotic agent, increasing fecal water content. Polyethylene glycol 3350 without electrolytes is supplied as a powder (MiraLax; Braintree Laboratories, Braintree, Mass) that is palatable when dissolved in a beverage such as water or juice.

Recent studies in adults have reported short-term efficacy of PEG without any major clinical adverse effects. Polyethylene glycol has been approved by the Food and Drug Administration for the short-term treatment of constipation in adults. Three small pediatric studies have reported short- and long-term efficacy of PEG. Polyethylene glycol is widely used in clinical practice for children with constipation, but, to our knowledge, there are no data on the long-term safety profile of this relatively new laxative in children or in adults. Therefore, the aim of our study was to assess the biochemical and clinical safety profile of long-term PEG treatment in a large cohort of children. We also assessed pediatric patient acceptance of long-term PEG therapy.
Characteristics of 83 Patients at Time of Evaluation*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female, No.</td>
<td>48/35</td>
</tr>
<tr>
<td>Age, y</td>
<td>7.4 (2.0-16.9)</td>
</tr>
<tr>
<td>Constipation duration, mo</td>
<td>28.8 (3-96)</td>
</tr>
<tr>
<td>Constipation, No.</td>
<td></td>
</tr>
<tr>
<td>Constipation only (&lt;4 years old)</td>
<td>15</td>
</tr>
<tr>
<td>Constipation only (&gt;4 years old)</td>
<td>29</td>
</tr>
<tr>
<td>With encopresis (&gt;4 years old)</td>
<td>39</td>
</tr>
<tr>
<td>Previous treatment, No.</td>
<td></td>
</tr>
<tr>
<td>No therapy</td>
<td>15</td>
</tr>
<tr>
<td>1 Medication</td>
<td>31</td>
</tr>
<tr>
<td>Multiple medications</td>
<td>37</td>
</tr>
<tr>
<td>PEG dose, g/kg per day</td>
<td>0.75 (0.2-1.8)</td>
</tr>
<tr>
<td>PEG solution volume, mL per day</td>
<td>267 (60-720)</td>
</tr>
<tr>
<td>PEG therapy duration, mo</td>
<td>8.7 (3-30)</td>
</tr>
<tr>
<td>PEG therapy &gt;12 mo, No.</td>
<td>21</td>
</tr>
</tbody>
</table>

Abbreviation: PEG, polyethylene glycol 3350 (MiraLax; Braintree Laboratories, Braintree, Mass).

*Data are given as mean (range) unless otherwise indicated.

low-up clinic visits from May 1, 2001, to September 30, 2002. None of the children from our 2 previous studies6-9 were included. The diagnosis of chronic constipation was based on symptoms of at least 3 months' duration, including at least 2 of the following symptoms: hard stools, painful defecation, encopresis, or fewer than 3 bowel movements per week. Patients with constipation were excluded if they had history of Hirschsprung disease, anorectal malformations, or any systemic illness potentially leading to constipation.

This study was approved by the institutional review board of the University of Iowa College of Medicine, Iowa City. Informed consent was obtained from parents of all patients, and assent was obtained from children older than 7 years.

PEG THERAPY

Following the diagnosis of constipation, PEG therapy was initially prescribed at the dose of 0.8 g/kg per day, based on our previous study, and all other laxative treatments were stopped. According to manufacturer's directions, parents were instructed to dissolve 17 g of PEG powder in 240 mL of water or other beverage and to give the prepared solution in 2 divided doses. Families were allowed their choice of beverage to suit each child's preference. Parents were asked to adjust the dose of PEG solution as required to yield 2 soft painless stools per day. Over time, parents were instructed to gradually decrease the dose of PEG if symptoms of constipation and encopresis showed improvement.

STUDY DESIGN

At the time of evaluation, parents were interviewed using a structured questionnaire and were asked about the dose of PEG given, medication compliance, beverage used to prepare PEG, and ease of mixing. Children were asked about liking the medication and preference compared with laxatives used in the past. Parents were asked about any possible adverse effects of PEG, and particularly about excessively loose or frequent stools, abdominal pain, flatulence, bloating, and nausea. Parents were asked about overall improvement in bowel movement pattern regarding stool frequency and consistency with PEG therapy.

Following the interview and physical examination, 4 mL of blood was obtained for measurement of levels of hemoglobin, hematocrit, serum electrolytes (including sodium, potassium, chloride, and carbon dioxide), blood urea nitrogen, serum creatinine, osmolality, albumin, aspartate aminotransferase, and alanine aminotransferase (ALT). Results of blood tests were considered abnormal if they were outside (even by 1 point) the age- and sex-appropriate reference range established in our hospital. If the results were abnormal, the blood tests were repeated within 8 weeks while the patient continued to receive therapy.

RESULTS

A total of 83 children (44 with constipation and 39 with constipation and encopresis) were enrolled in the study. The patient characteristics are given in the Table. Previous therapy for constipation was attempted in 68 children (82%), and 37 of them had received multiple medications. The previous treatment regimens included milk of magnesia in 64 patients (77%); mineral oil, 19 (23%); frequent suppositories or enemas, 17 (20%); senna, 16 (19%); fiber in various forms, 11 (13%); docusate sodium, 7 (8%); and others. At the time PEG therapy was started, patients were symptomatic, and most were taking laxatives either inconsistently or in inadequate doses.

PEG SAFETY

Clinical adverse effects of PEG therapy were minor and acceptable over the mean duration of 8.7 months (range, 3-30 months) of PEG therapy. Eight patients (10%) reported frequent watery stools sometime during therapy. The diarrhea disappeared with reduction of the dose. Other adverse effects reported were bloating or flatulence in 5 children (6%) and abdominal pain in 2 children (2%). Thirst, fatigue, and nausea after receiving PEG solution on an empty stomach were reported in 1 patient each (1%). None of the patients stopped treatment due to adverse effects, and all were willing to continue PEG therapy. The general physical examination findings revealed no new significant abnormalities compared with the pretreatment examination in all children.

The laboratory evaluation results, including measures of hemoglobin, hematocrit, serum electrolytes, blood urea nitrogen, serum creatinine, serum albumin, and osmolality, were normal in all patients. Ten patients did not have serum osmolality measured. Nine patients (11%) had a slightly elevated ALT level (<1.5 times the upper limit of normal; range, 31-45 U/L). Eight of these patients had ALT levels remeasured within 8 weeks, 7 of whom were still receiving PEG therapy. Seven of these 8 patients had values in the reference range, while 1 had a slightly elevated ALT level (<1.2 times normal; 28 U/L). Three patients (4%) had an elevated aspartate aminotransferase level (<1.5 times normal; range, 42-52 U/L), and all had normal values when remeasured while still receiving PEG therapy. The dose and duration of PEG therapy were not significantly different in the patients with abnormal values compared with those with laboratory values in the reference range.

PATIENT ACCEPTANCE

Polyethylene glycol was mixed in any beverage to suit the child's preference. Forty-one children used fruit juice (49%);
Chronic constipation is a common problem in children and requires long-term treatment with laxatives. Polyethylene glycol 3350 is a newly available laxative that is widely used in children. Recent studies report efficacy of PEG, but data on its long-term use and safety are lacking.

This study reports a lack of major clinical adverse effects and biochemical abnormalities in a large cohort of children receiving PEG 3350 therapy over the long-term. The study also reports good patient acceptance and compliance with PEG therapy. Polyethylene glycol 3350 should be considered as a favorable therapeutic option for children with chronic constipation with or without encopresis because of its safety and efficacy over the long term and good patient acceptance.

In our study, long-term PEG therapy did not have any major clinical adverse effects. The most common clinical adverse effect was excessively loose or frequent stools that resolved with reduction of the PEG dose. Other adverse effects were minimal and acceptable. Polyethylene glycol does not ferment by colonic bacterial flora and, therefore, does not cause excessive gas production that other laxatives do.

PEG solution was well liked by 78 children (93%). All 68 children who had used other therapies preferred PEG to other laxatives. Daily compliance, assessed by parent recall and diary, was good in 75 patients (90%) during the mean duration of 8.7 months of therapy. Seventy-eight (91%) of 83 caretakers reported definite improvement in bowel movement pattern with PEG therapy.

**What This Study Adds**

Constipation with or without encopresis is often a chronic problem in children. In one long-term study from the United States, 37% of children continued to have symptoms of constipation 3 to 12 years after initial diagnosis. In another study from Italy, constipation persisted in 52% of children 5 years after initial diagnosis. Adequate doses of laxatives and treatment compliance are the most important factors for successful resolution of chronic constipation. Long-term treatment is required for children with chronic constipation, as relapse is common after premature discontinuation of laxatives. Therefore, there is a need for an ideal laxative that is safe, effective, and acceptable to children over the long-term.

In our study, long-term PEG therapy did not have any major clinical adverse effects. The most common clinical adverse effect was excessively loose or frequent stools that resolved with reduction of the PEG dose. Other adverse effects were minimal and acceptable. Polyethylene glycol does not ferment by colonic bacterial flora and, therefore, does not cause excessive gas production that leads to flatulence or bloating. Polyethylene glycol 3350 is a newly available laxative that is widely used in children. Recent studies report efficacy of PEG, but data on its long-term use and safety are lacking.

This study reports a lack of major clinical adverse effects and biochemical abnormalities in a large cohort of children receiving PEG 3350 therapy over the long-term. The study also reports good patient acceptance and compliance with PEG therapy. Polyethylene glycol 3350 should be considered as a favorable therapeutic option for children with chronic constipation with or without encopresis because of its safety and efficacy over the long term and good patient acceptance.

In summary, PEG seems to be a safe medication for long-term treatment of constipation in children. It should be considered a favorable option for long-term therapy for children, particularly because of excellent patient acceptance.
Accepted for publication February 6, 2003.
This study was financially assisted by Braintree Laboratories.
We thank Aliye Uc, MD, Dawyn Sawyer, MPAS, and Judith Heckman, MPAS, for their assistance in the study.
This study was presented in part at the American Gastroenterological Association Meeting; May 20, 2002; San Francisco, Calif. This study was published as an abstract in Gastroenterology (2002:122[suppl]:A318).

Corresponding author and reprints: Dinesh Pashankar, MD, Division of Gastroenterology, 2864 John Pappajohn Pavilion, Children's Hospital of Iowa, 200 Hawkins Dr, Iowa City, IA 52242 (e-mail: Dinesh-Pashankar@uiowa.edu).

REFERENCES