

Clinical efficacy and safety of polyethylene glycol 3350 versus liquid paraffin in the treatment of pediatric functional constipation

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ABSTRACT

Background and the purpose of the study: Functional constipation is prevalent in children. Recently polyethylene glycol has been introduced as an effective and safe drug to treat chronic constipation. There are only a few clinical trials on comparison of PEG and liquid paraffin in childhood constipation. The purpose of this study was to evaluate clinical efficacy and safety of PEG 3350 solution and liquid paraffin in the treatment of children with functional constipation in Sari Toba clinic during the period of 2008-2009.

Methods: Children with a history of functional constipation were subjects of this study. One hundred and sixty children of 2-12 years old with functional constipation were randomized in two PEG and paraffin treatment groups. Patients received either 1.0-1.5 g/kg/day PEG 3350 or 1.0-1.5 ml/kg/day liquid paraffin for 4 months. Clinical efficacy was evaluated by stool and encopresis frequency/week and overall treatment success rate was compared in two groups.

Results and major conclusion: Compared with the baseline, defecation frequency/ week increased significantly and encopresis frequency meaningfully decreased in two groups during the period of the study. Patients using PEG 3350 had more success rate (mean: 95.3%±3.7) compared with the patients in paraffin group (mean: 87.2%±7.1) ($p=0.087$). Administration of PEG 3350 were associated with less adverse events than liquid paraffin. In conclusion in treatment of pediatric functional constipation, regarding clinical efficacy and safety, PEG 3350 were at least as effective as liquid paraffin and but less adverse drug events.

Keywords: Defecation, Encopresis, Lactulose, Mineral oil.

INTRODUCTION

Approximately 3% of general pediatric outpatient visits and 25% of pediatric gastroenterology consultations are related to perceived defecation disorders (1). More than 95% of children older than 1 year with constipation suffer from functional constipation (2). Liquid paraffin (mineral oil) is widely accepted and recommended as a fundamental component of regimens for the management of constipation in North America and Australia (3). Extensive experiences with long-term uses of mineral oil have shown its efficacy and safety (4) and North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGN) clearly identify liquid paraffin as a medication of first choice in the management of pediatric constipation (3). This drug combines ease of titration with tolerability and sustained effect despite prolonged uses and make it attractive for use in childhood constipation encopresis (5). Mineral oil is not recommended for infants less than 1 year old due to the risk of aspiration and development of lipoid pneumonia.

Some studies have shown PEG has at least equal efficacy and fewer adverse effects in comparison with lactulose (6, 7). A recent systematic review has demonstrated the efficacy of PEG as good as or even better than lactulose or milk of magnesia over a wide range of ages and treatment durations (8). There are only a few clinical trials on the comparison of PEG and liquid paraffin in childhood constipation. The purpose of this study was to evaluate clinical efficacy and safety of PEG 3350 solution and liquid paraffin in the treatment of children with functional constipation.

METHODS

Subjects

Patients eligible for enrolment were ambulatory 2 to 12 years old children with a history of functional constipation (at least 3 months) defined as less than 3 stools/week, more than 1 encopresis/week or palpable abdominal or rectal fecal mass on physical examination. The patients referred to Toba clinic

Table 1. Baseline characteristics of the patients.

Variable	PEG 3350	Paraffin	P value
Gender (male/female)	41/39	43/35	0.625
Age (month)	52.8±23.4	50.6±23.6	0.56
Fecal impaction	42	40	0.94
Rectal bleeding during defecation	11	13	0.61
Pain during defecation	71	70	0.84

initially were examined and followed during the study by a pediatric gastroenterologist.

Exclusion criteria were: Withdrawn the treatment during the first month, hypothyroidism, Hirschsprung disease; known cardiac, renal and neurologic disorders, any sign of organic causes, and history of colon surgery. At the time of enrolment, a full history details was obtained including pain or bleeding during defecation, frequency of defecation, fecal impaction, and encopresis. Written informed consent was obtained from parents after full description of the study details. The ethics committee of Mazandaran University of Medical Sciences (MAZUMS) approved this open-labeled randomized study that accomplished in Sari Toba clinic affiliated to MAZUMS during the period of 2008-2009. At the beginning of the therapy, all patients and their parents were educated for appropriate diet, dairy consumption, toilet training and adverse drug reactions. Random table was used to randomize the patients in two groups.

Study Protocol

Patients were randomly assigned to receive either 1.0-1.5 g/kg/day PEG 3350 or 1.0-1.5 ml/kg/day liquid paraffin orally for 4 months. PEG 3350 powder was prepared as a 40% solution to trust reliable to apply the pediatric dosing and to increase compliance and liquid paraffin was provided from a pharmaceutical factory. For rectal disimpaction, bisacodyl suppositories were applied at the beginning of the study. After the first physical exam, the patients were visited at least on the days of 7, 14, 30, 60, 90, and 120 during the treatment period, repeatedly.

Assessment

Clinical efficacy was evaluated by stool and encopresis frequency/week and overall treatment success rate was compared in two groups. Patients that were withdrawn from the study due to lack of efficacy or adverse reaction of the drug placed in unsuccessful cases and remaining were considered as successful group. Adverse drug events were determined during examination or at the time of complain of patients and their parents.

Statistical Analyses

The statistical analysis was performed using SPSS-16 software and results were expressed as

means±SD. Means differences between two groups were compared by independent samples t-test. P-values less than 0.05 were considered statistically significant.

RESULTS AND DISCUSSION

One hundred and sixty children 2-12 years old with functional constipation were included in this study. Since 2 patients dropped out in paraffin group, the final data were reported of a total 158 patients (80 in the PEG and 78 in the paraffin groups). There was no significant difference with regard to age, and baseline frequencies of stool, encopresis, fecal impaction, rectal pain or bleeding during defecation between two treatment groups Table 1.

Although all patients and their parents were educated for appropriate diet, dairy consumption and toilet training initially and during the study, the amount of patients' compliance were not recorded and compared.

This randomized clinical trial demonstrated that both PEG 3350 and liquid paraffin were effective in increasing defecation frequency and decreasing encopresis significantly during the 4 month treatment period. The mean defecation rate significantly increased in PEG group from 1.6 ± 0.8/week to 7.0 ± 3.8/week and 1.4 ± .05/week to 6.3 ± 3.1/week in paraffin group (Table2). Patients using PEG and liquid paraffin had less encopresis in the 30th day of the treatment (from 27 cases to 12 and 28 cases to 10 in two groups respectively, $p>0.05$). As a result, with regard to defecation and encopresis frequency, PEG 3350 and liquid paraffin were equally effective.

Success rates were compared at 30, 60, 90 and 120 days after the beginning of the therapy and are shown in figure 1. A higher number of patients in the PEG group (mean: 95.3%±3.7) were treated compared with the paraffin group (mean: 87.2%±7.1) ($p=0.087$). Although the mean differences were not significant, the trend of success rate showed that larger sample size could demonstrate better efficacy.

For the significant number of children with chronic constipation, maintenance therapy may be essential for longer period to regulate bowel movements without difficulty. A few studies have been performed to compare PEG vs. paraffin with regards to clinical efficacy and safety.

A crossover randomized clinical trial in 37 patients

Table 2. Number of defecation/week at the beginning and during the treatment in two groups.

Time	PEG 3350 (Mean±SD)	Paraffin (Mean±SD)	P value
At the beginning	1.6±0.8	1.4±0.5	0.69
7 th day	4.1±1.7	3.3±0.8	0.19
14 th day	6.1±3.7	5.1±1.9	0.54
30 th day	7.0±3.8	6.3±3.1	0.70
60 th day	9.1±3.7	7.6±3.8	0.49
90 th day	8.9±3.8	7.6±3.4	0.51
120 th day	8.7±2.9	7.5±3.2	0.58

Table 3. Incidences of adverse drug reactions using PEG 3350 and paraffin.

Adverse reaction	PEG 3350 (Mean±SD)	Paraffin (Mean±SD)	P value
Nausea	4.5±2.4	12.3±2.6	<0.01
Vomiting	0.2±0.4	2.5±1.9	0.014
Diarrhea	2±1.7	3.5±2.2	0.209
Flatulence	3.8±1.5	10.8±1.6	<0.01
Abdominal pain	1.7±0.8	6.0±1.9	<0.01
Dehydration	0.0±0.0	0.5±0.5	0.049
Withdraw for ADR	0.3±0.5	1.5±1.1	0.035
Withdraw for no efficacy	0.8±0.9	1.2±1.1	0.61
Need to additive drugs	1.2±1.1	2.2±1.5	0.22

aged 2 to 16 years, PEG 3350 and lactulose increased stool frequency from 1.7±0.8/week to 14.8±1.4/week and 13.5±1.5/week respectively (6). Administration of PEG at the average dose of 1g/kg/day to 75 children 1-24 months with constipation increased mean defecation frequency from 3.7±3.2/week to 12.4±7.0/week in the initial 4 month of therapy (10). In a similar study, 74 children with chronic constipation, mentioned stool frequency increased significantly with PEG (from 2.8±0.3/week to 9.9±0.7/week) ($p<0.001$) (11). Significant decrease in the mean encopresis frequency/week was found in a study in Netherland (7). Similarly Karami et al reported that PEG 4000 was more effective than oral paraffin to increase stool frequency (from 2.6±1.4/week to 4.7±1.8/week and 3.0±1.5/week to 4.5±1.9/week respectively) (12).

In a case control study (13), children with constipation were treated with PEG or milk of magnesia. During one year follow up, bowel movement frequency increased and soiling events decreased significantly in both groups. In another report PEG 3350 and lactulose were compared in 100 children 6 months to 15 years with functional constipation for 8 weeks (7). It was found that 56% in PEG group were successfully treated compared to 29% in lactulose group and there were significant increase in the mean stool frequency/week and decrease encopresis frequency/week in

both groups. A 3-month study with 96 patients aged 6-36 months showed the efficacy of PEG 4000 equal to or greater than lactulose (14).

A 2-week crossover study using either PEG 3350 or lactulose, reported that the success rate was significantly higher in PEG group (84%) than lactulose group (46%) (6). Also the treatment with PEG was more effective in terms of tolerability. Wang et al in their 2 weeks study have shown PEG 4000 is meaningfully more effective than lactulose (70% vs. 40%) (15). A randomized study that compared PEG 3350 without electrolytes with milk of magnesia for constipation and fecal incontinence concluded that PEG and milk of magnesia were equally effective in long-term treatment. (16)

All of adverse reactions (nausea, vomiting, flatulence, abdominal pain and dehydration), other than diarrhea, occurred more frequently in patients using liquid paraffin compared with PEG 3350 ($p<0.05$) (Table 3). Rate of withdrawn for ADRs in those using paraffin were significantly higher than PEG 3350 ($p<0.05$).

In agreement with results of other reports (10, 13, 17-18), in the present study, patients or their parents addressed mild adverse events and did not report any serious or new onset adverse reactions. In an eight weeks study period (7) PEG 3350 had no serious or significant adverse events and less adverse reactions

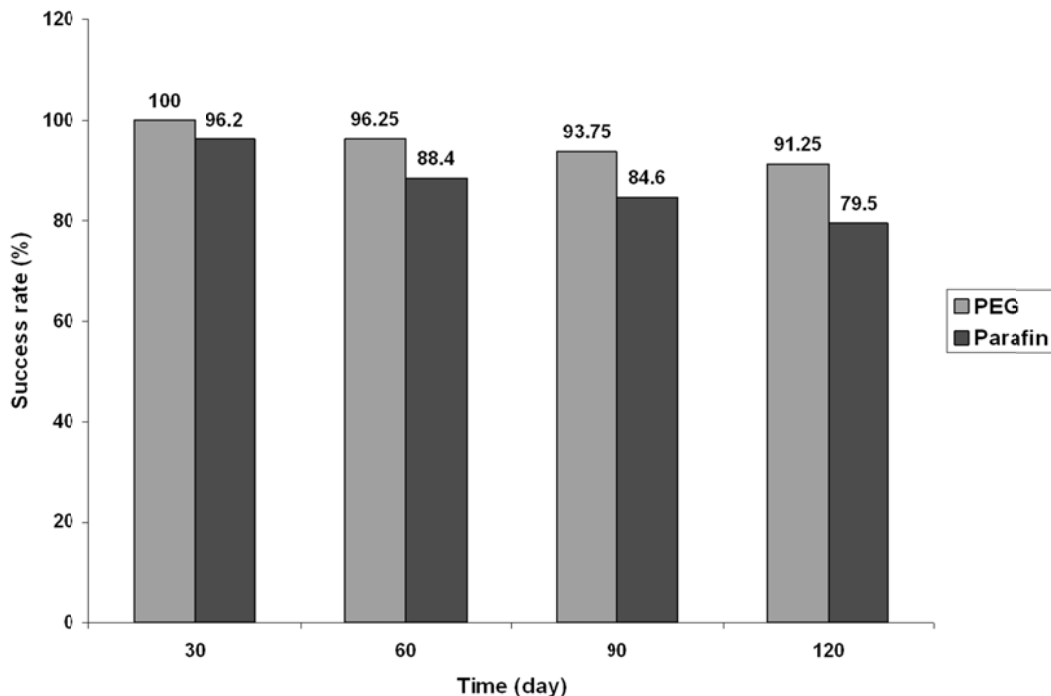


Figure 1. Rate of the success (%) in the course of the treatment for two groups.

occurred compared with patients using lactulose. Although it has been reported that liquid paraffin is more effective with fewer side effects, (17, 19), the present study showed that treatment of chronic constipation with PEG 3350 had less adverse events compared with liquid paraffin. These results were similar to others that reported PEG was safe for long term treatment of children with constipation. (16, 18).

CONCLUSION

The results of this study demonstrated that PEG 3350 was at least as effective as liquid paraffin to

treat pediatric functional constipation and with less adverse drug events. Reviewing the results of the present investigations and other studies with regard to clinical efficacy and safety, revealed that PEG 3350 can be drug of choice for treatment of chronic constipation in majority of children.

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