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Original Article

Comparison of the effect of polyethylene glycol 40% and fig syrups on the treatment of chronic functional constipation in children: A randomized clinical trial

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Abstract

Background and aims: None of the available constipation treatments for children are completely successful. Therefore, the present study aimed to evaluate the effect of the polyethylene glycol (PEG) solution 40% and fig syrup on the treatment of chronic constipation in children.

Methods: In this double-blind clinical trial, 120 patients with chronic functional constipation were selected and divided into two groups. The first group received 5 mL of fig syrup without senna 3 times daily, and the second group took PEG 40% syrup at 1 mL/kg of body weight per day (the dose was adjustable according to the patient's condition and need). At weeks 0, 2, 4, and 6, a checklist containing questions about children's constipation was completed by the researcher, and the data were analyzed by SPSS version 24.

Results: Changes in the frequency of abdominal pain at fourth times 0, 2, 4, and 6 weeks demonstrated statistically significant differences between the two groups ($P=0.044$), and it was significantly lower the in PEG group; however, the defecation was not statistically significant ($P=0.902$). After six weeks, the frequency of painful defecation, difficult defecation straining during defecation, and fear of defecation was significantly lower in the group given PEG syrup compared to the fig syrup-receiving group ($P=0.001$).

Conclusion: Overall, PEG syrup was significantly effective in treating chronic functional constipation in children compared to the fig syrup.

Keywords: Constipation, Polyethylene glycol, Children, Fig syrup

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Introduction

Constipation is a common problem in childhood that is hard to diagnose due to the presence of various symptoms such as delayed defecation, difficult defecation, and fecal incontinence, which are due to the formation and retention of impacted stool in the rectum (1). The term functional constipation is mainly used to describe constipation without organic etiology. Many children with functional constipation have fecal incontinence with a variable prevalence of 18-89% and a mean of 40%-60% (2). This disease is observed in all social classes and has various causes such as genetic predisposition, low fiber intake, socioeconomic status, lack of sufficient fluid intake, and lack of exercise (3). Functional constipation reduces the quality of life in children (4), and fecal incontinence in these patients can adversely affect therapeutic outcomes (5). It is noteworthy that laxative therapy alone cannot guarantee the treatment of functional constipation, and dietary recommendations such as reducing milk consumption and increasing the consumption of solid foods with high fiber content, as well as toilet training play an important role in the success of medical treatment (6).

The common fig (*Ficus carica* L.) has 600 species, most of which are wild or ornamental, including the rubber tree known as *Ficus elastica* L., which is an ornamental and industrial type. *Ficus benghalensis* L. and *Ficus religiosa* L. are the ornamental types of this plant, which are used in decorations and as a houseplant. Species used in gardening for their fruits include *F. carica* L. and *Ficus palmata* L (7). *F. carica* is applied as a fruit, and butut *Ficus palmata* L. and *Ficus podocarpus* L. are mainly cultivated for the fertilization of various types of edible figs. According to research evidence, the leaves of a fig tree are used for their digestive properties, intestinal worms, pain relief, as boiled, and for cough. Fig fruit is also used to soften the chest and facilitate defecation. Therefore, syrups containing figs have been developed for the treatment of constipation in children in the pharmaceutical market by both Iranian and foreign pharmaceutical companies (8,9).

Polyethylene glycol (PEG) is a water-soluble polymer with a high molecular weight that can form hydrogen bonds with 100 molecules of water per molecule of PEG. When PEG is orally consumed, it hydrates the contents of the colon and facilitates intestinal passage and painless defecation as a linear curve in a dose-dependent manner (10,11). Therefore, PEG-based laxatives can be more useful for complete feces excretion compared to rectal prescriptions (12).

PEG is usually administered at a concentration of 40% in children. Given the lack of uniform uptake of the drug in the powder form at a specific dose and that the availability of an appropriate base for preparing 40% PEG syrup can assist in establishing drug stability and appropriate dosage, as well as fig's appetizing and laxative effect. In addition, fig syrup can be used as a base for 40% PEG syrup due to its desirable taste (13,14). Taking into account the above-mentioned discussion, we decided to comparatively investigate the effects of PEG and fig syrups on the treatment of chronic functional constipation.

Materials and Methods

Study design and setting

This double-blind clinical trial was conducted in a university-affiliated clinic in Shahrekord in 2018.

Sample size calculation

Using the following formula and taking into account a 95% confidence interval and 80% test power, the sample size in each group was equal to 51. Considering the loss of 61 people in each group, two people declined to participate in the study, and finally, a total of 120 people were enrolled in the study (Figure 1).

The sample size was computed at 60 for each group according to similar research (15) and the formula for sample size calculation.

$$n = \frac{2(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta})^2 \sigma^2}{d^2}$$

Inclusion and exclusion criteria

The inclusion criteria were suffering from chronic functional constipation, being within the age range of 2-10 years, having no large and small intestinal diseases, having no allergy to fig or PEG, having no bowel obstruction, and not suffering from kidney failure and heart failure. On the other hand, the exclusion criteria included diarrhea following drug administration and unwanted allergic reactions after drug administration.

Intervention

After the approval of the study protocol by the Ethics Committee of the University, a total of 120 patients with chronic functional constipation referring to Imam Ali Clinic were selected based on the inclusion and exclusion criteria and randomly assigned to two groups each containing 60 patients.

To prepare fig syrup, the hydroalcoholic extract of dried white fig powder and the dry extract were prepared, respectively. Then, fig syrup 25% was prepared by calculation. Fig syrup base was used to prepare PEG 40% syrup base by calculating the final solvent.

The first group received 5 mL of fig syrup daily three times a day. The second group was given 1 mL/kg of body weight of PEG 40% syrup (dosage was adjustable according to the patient's condition and need) per day. A researcher-made checklist was completed in weeks 0, 2, 4, and 6, and the data were analyzed by appropriate statistics.

Randomization and blinding

All the drugs provided to the researcher had the same

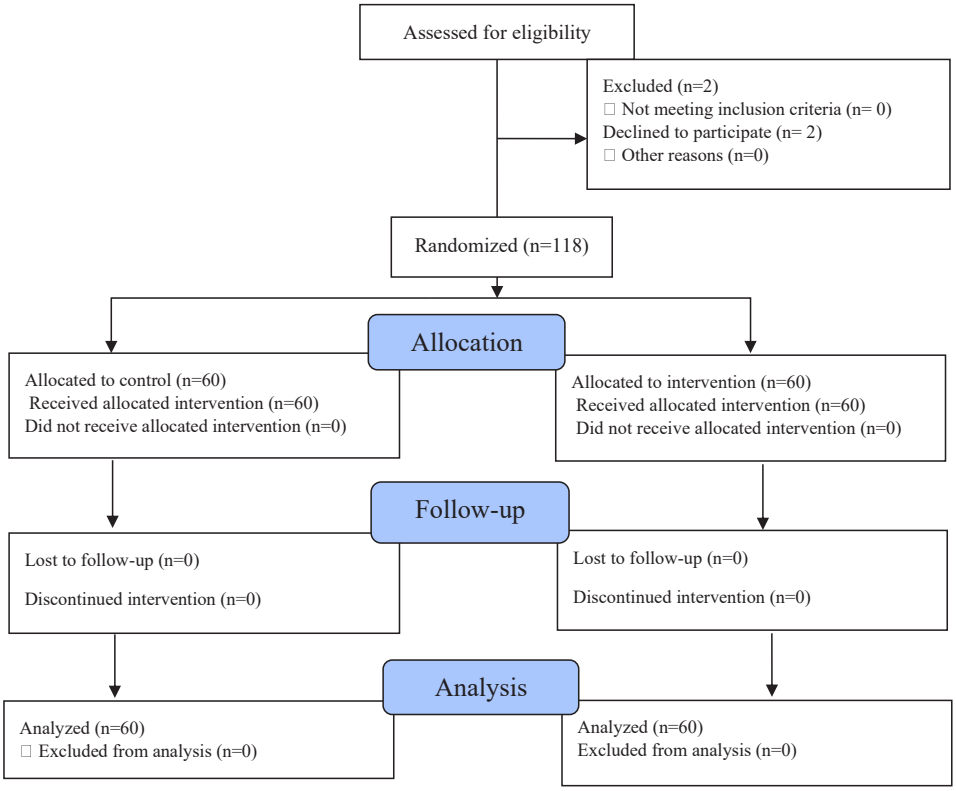

Figure 1. CONSORT flow diagram of the study population.

label and were labeled by a consultant pharmacist. For randomization, two cards with different colors were placed in front of the patient, and the patient chose one. Each color represented one of the two solutions. The patient's information form was also kept by the medical secretary and was not disclosed to the physician or researchers.

Safety measures

All parents of children were asked open-ended questions about any possible allergic or adverse reactions in their children.

Data analysis

Data were collected using SPSS, version 24. The mean and standard deviation (SD), as well as frequency and percentage, were used to describe quantitative and qualitative data, respectively. Further, the chi-square test and one-way analysis of variance (ANOVA) were applied to compare qualitative and quantitative data, respectively, and $P<0.05$ was considered a significant level.

Results

There was no significant difference between the two groups in terms of age, age at the onset of the disease, birth weight, weight, parental education level, disease history, and hospitalization history, as well as the frequency of hospitalizations, medication history, history of allergy, urinary tract infection, and a family history of constipation (Table 1).

Table 1. Comparison of demographic characteristics of patients in the studied groups

Variable	Group	Fig syrup (n=60)	PEG syrup (n=60)	*P* value
Disease history	No	45 (75)	43 (71.7)	0.685[a]
	Gastrointestinal	5 (8.3)	8 (13.3)	
	Infectious	5 (8.3)	2 (3.3)	
	Heart	2 (3.3)	3 (5)	
	Miscellaneous	3 (5)	4 (6.7)	
Hospitalization history	No	29 (49.2)	28 (46.7)	0.919[a]
	Gastrointestinal diseases	11 (18.6)	11 (18.3)	
	Non-gastrointestinal diseases	16 (27.1)	15 (25)	
	Miscellaneous	3 (5.1)	5 (8.3)	
Frequency of hospitalizations	No	29 (49.2)	28 (45.9)	0.944[a]
	1-2	28 (47.5)	30 (50)	
	3-4	2 (3.4)	2 (3.3)	
Medication history	No	24 (40)	19 (31.66)	0.833[a]
	Pidrolax	13 (21.7)	18 (30.14)	
	Fig syrup	3 (5)	5 (8.3)	
	Lactulose	11 (18.3)	11 (18.3)	
	Magnesium hydroxide 5	4 (6.7) 5 (8.3)	2 (3.3) 5 (8.3)	
Urinary tract infection	No	44 (75.9)	43 (71.7)	0.529[a]
	Once	13 (22.4)	17 (28.3)	
	Twice	1 (1.7)	0 (0)	
Allergy	No Drug Food	52 (86.7) 8 (13.3) 0 (0)	51 (85) 6 (10) 3 (5)	0.305[a]
Family history of constipation	No Yes	14 (23.7) 45 (76.3)	14 (23.7) 45 (76.3)	>0.99
Mother's education level	Illiterate Elementary Under high school diploma high school diploma and higher	0 (0) 2 (3.3) 11 (18.3) 47 (78.3)	1 (1.7) 0 (0) 8 (13.3) 51 (85)	0.294[a]
Father's education level	Illiterate Elementary Under high school diploma high school diploma and higher	0 (0) 1 (1.7) 14 (23.3) 45 (75)	1 (1.7) 1 (1.7) 15 (25) 43 (71.7)	0.916[a]
Age (year)		2.36±5.15	2.11±4.79	0.382
Age at the onset of the disease (year)		2.13±2.71	1.73±2.17	0.139
Birth weight (kg)		0.62±3.14	0.55±3.19	0.697
Weight (kg)		10.12±19.46	8.97±18.65	0.650

Values are expressed as frequency (%) and mean (±SD) for qualitative and quantitative variables, respectively. An independent *t* test was used to analyze quantitative variables, and Chi-square [(a)] and Fisher's exact test were employed to analyze qualitative variables.

The majority of both groups had a history of the consumption of vegetables, juices, milk-yogurt, and water, and both groups had physical activities. There was no significant difference in nutrition-related and physical activity characteristics between the groups (Table 2).

The results of the repeated-measures analysis of variance showed that changes in the defecation rate at fourth times of 0, 2, and 4, 6 weeks were not statistically significant in the two groups ($P=0.902$). Based on the test results, there was a significant difference between fig ($P=0.001$) and PEG ($P=0.001$) syrup groups in the defecation rate in each of the groups in the studied times. In addition, based on the results of the repeated-measures analysis of variance, changes in the frequency of abdominal pain at fourth times 0, 2, 4, and 6 weeks were statistically different between the two groups ($P=0.044$). The frequency of abdominal pain changes in the fig syrup group was more than that of the PEG syrup group. Moreover, the test results demonstrated that changes in the frequency of abdominal pain in the studied times were significantly different between fig ($P=0.001$) and PEG ($P=0.001$) syrup groups (Table 3).

The experiences of defecation-related problems at the studied intervals revealed that the frequency percentage of fecal incontinence at 2, 4, and 6 weeks post-intervention in the two groups was approximately similar ($P=0.540$, $P=0.157$, and $P=0.107$, respectively).

Although the frequency of painful defecation, straining during defecation, and fear of defecation in the two groups was almost the same at baseline, it was significantly lower in the group given PEG syrup compared to the fig syrup-receiving group at weeks 2, 4, and 6 post-intervention.

Based on the findings, the frequency of difficult defecation at all intervals (baseline and 2, 4, and 6 weeks post-intervention) was lower in the PEG syrup-receiving group in comparison with the fig syrup-given group ($P=0.001$). The frequency of blood in stool at week 4 post-intervention was lower in the group given PEG syrup compared to the fig syrup-receiving group ($P=0.004$), but it was nearly similar at other intervals (Table 4).

Discussion

The present study sought to investigate the effects of PEG and fig syrups on the treatment of chronic functional constipation in children.

The findings of the current study represented no relationship between age and treatment response. Several other studies reported that responding to different treatments such as PEG and lactulose is not significantly different among different age groups such as those under and over 6 years (2,16,17).

Oh et al concluded that there was a significant difference in nutrient absorption and consumption, water absorption and consumption, body weight, and blood test results between treatments with induced constipation and those

Table 2. Comparison of nutrition-related and physical activity characteristics of patients in the studied groups

Variable		Group		*P* value
		Fig syrup (n=60)	PEG syrup (n=60)	
		No. (%)	No. (%)	
Vegetable consumption	No	13 (21.7)	16 (26.7)	0.522
	Yes	47 (78.3)	44 (73.3)	
Juices consumption	No	24 (40)	23 (38.3)	0.852
	Yes	36 (60)	37 (61.7)	
Milk-yogurt consumption	No	11 (19.6)	5 (8.3)	0.078
	Yes	45 (80.4)	55 (91.7)	
Water consumption	No	3 (5)	0 (0)	0.244[a]
	Yes	57 (95)	60 (100)	
Physical activity	No	3 (5)	4 (6.7)	>0.99[a]
	Yes	57 (95)	56 (93.3)	

Note. PEG: polyethylene glycol.
[a] Fisher's exact test; The Chi-square test was used for the other variables.

Table 3. Comparison of mean bowel movements and abdominal pain in fig syrup and PEG Syrup groups

Group Variable		Fig syrup (n=60)	PEG syrup (n=60)	*P* value
		Mean ± SD	Mean ± SD	
Defecation rate	Baseline	3.15±1.97	2.70±1.77	0.241
	Second week	3.80±1.53	4.13±2.08	0.579
	Fourth week	4.58±1.36	4.63±1.89	0.994
	Sixth week	5.97±1.26	6.15±1.47	0.279
Repeated measures analysis in each group		0.001	0.001	
Repeated measures analysis in both groups		0.902		
Frequency of abdominal pain	Baseline	4.00±2.74	3.67±2.62	0.425
	Second week	3.03±2.41	2.08±2.14	0.034
	Fourth week	2.37±2.20	1.58±1.84	0.041
	Sixth week	1.55±1.86	0.87±1.31	0.037
Repeated measures analysis in each group		0.001	0.001	
Repeated measures analysis in both groups		0.044		

Note. PEG: Polyethylene glycol; SD: Standard deviation.

Table 4. Comparison of the frequency of defecation-related problems in fig syrup and PEG syrup groups

Variable			Group		*P* value
			Fig syrup (n=60)	PEG syrup (n=60)	
			No. (%)	No. (%)	
Fecal incontinence	Baseline	With	22 (36.7)	24 (40)	0.707
		Without	38 (63.7)	37 (60.7)	
	Second week	With	18 (30)	15 (25)	0.540
		Without	42 (70)	46 (75.4)	
	P value		0.103	0.002	
	Fourth week	With	14 (23.3)	8 (13.3)	0.157
		Without	46 (76.7)	53 (86.9)	
	P value		0.010	0.000	
	Sixth week	With	11 (18.3)	5 (8.3)	0.107
		Without	49 (81.7)	56 (91.8)	
	P value		0.004	0.000	
Painful defecation	Baseline	With	50 (83.3)	54 (90)	0.283
		Without	10 (16.7)	6 (9.8)	
	Second week	With	47 (78.3)	22 (36.7)	0.001
		Without	13 (21.7)	38 (62.3)	
	P value		0.083	0.000	
	Fourth week	With	43 (71.7)	13 (21.7)	0.001
		Without	17 (28.3)	48 (78.7)	
	P value		0.007	0.000	
	Sixth week	With	23 (38.3)	5 (8.3)	0.001
		Without	37 (61.7)	56 (91.8)	
	P value		0.000	0.000	
Difficult defecation	Baseline	With	60 (100)	54 (88.5)	0.013a
		Without	0	7 (11.5)	
	Second week	With	55 (91.7)	24 (40)	0.001
		Without	5 (8.3)	37 (60.7)	
	P value		0.024	0.000	
	Fourth week	With	48 (80)	15 (25)	0.001
		Without	12 (20)	46 (75.4)	
	P value		0.000	0.000	
	Sixth week	With	24 (40)	3 (5)	0.001
		Without	36 (60)	58 (95.1)	
	P value		0.000	0.000	
Blood in stool	Baseline	With	19 (31.7)	20 (33.3)	0.845
		Without	41 (63.8)	41 (67.2)	
	Second week	With	18 (30)	12 (20)	0.206
		Without	42 (70)	49 (80.3)	
	P value		0.327	0.004	
	Fourth week	With	12 (20)	2 (3.3)	0.004
		Without	48 (80)	59 (96.7)	
	P value		0.007	0.000	
	Sixth week	With	7 (11.7)	2 (3.3)	0.163a
		Without	53 (88.3)	59 (96.7)	
	P value		0.001	0.000	

Table 4. Continued

Variable			Group		*P* value
			Fig syrup (n=60)	PEG syrup (n=60)	
			No. (%)	No. (%)	
Straining during defecation	Baseline	With	58 (96.7)	58 (95.1)	>0.99a
		Without	2 (3.3)	3 (4.9)	
	Second week	With	56 (93.3)	38 (62.7)	0.001
		Without	4 (6.7)	23 (37.7)	
	P value		0.159	0.000	
	Fourth week	With	44 (73.3)	20 (33.3)	0.001
		Without	16 (26.7)	41 (67.2)	
	P value		0.000	0.000	
	Sixth week	With	28 (46.7)	7 (11.5)	0.001
		Without	32 (53.3)	54 (88.5)	
	P value		0.000	0.000	
Fear of defecation	Baseline	With	40 (66.7)	43 (71.7)	0.553
		Without	20 (33.3)	17 (27.9)	
	Second week	With	38 (63.3)	26 (43.3)	0.028
		Without	22 (36.7)	35 (57.4)	
	P value		0.159	0.000	
	Fourth week	With	29 (48.3)	16 (26.7)	0.014
		Without	31 (51.7)	45 (73.8)	
	P value		0.000	0.000	
	Sixth week	With	25 (41.7)	6 (9.8)	0.001
		Without	35 (58.3)	55 (90.2)	
	P value		0.000	0.000	

Note. PEG: Polyethylene glycol; SD: Standard deviation.
[a] Fisher's exact test; for the other variables, the Chi-square test.

containing fig paste (18), which is in line with the findings of the present study where there was no relationship between weight and treatments.

The results of the present study showed PEG syrup was significantly effective in treating chronic functional constipation in children compared to fig syrup; this was because it was more effective on abdominal pain, frequency of painful defecation, difficult defecation, straining during defecation, and fear of defecation. However, fig has antibiotics and antioxidants (18), and several studies approved that it has anti-constipation properties, but in this study, PEG syrup was preferable to fig syrup. For example, Kim et al (13) reported the therapeutic effect of figs against constipation. Likewise, Tajik et al conducted a study to comparatively investigate the effects of red sugar and fig syrup on functional constipation in children. Accordingly, 30 children received fig syrup and 30 children were given red sugar for four weeks. Their findings revealed that there was no significant difference between the effects of red sugar and fig syrup concerning the frequency of bowel movement and painful defecation. However, fig syrup had a better effect on inducing diarrhea and reducing anorexia and abdominal pain compared to red sugar, confirming the effect of fig syrup on the treatment of functional constipation in children (19).

In line with the present study, Treepongkaruna et al compared the effect of PEG and lactulose on the treatment of constipation in children by examining the frequency of bowel movements, as well as the facilitation of defecation in children and concluded that PEG had superior effects over lactulose (15). In a study on evaluating the clinical efficacy and safety of PEG, compared to liquid paraffin, for the treatment of functional constipation in children, the results indicated that the frequency of bowel movements per week significantly increased, while fecal incontinence significantly decreased in both groups. The success rate in the PEG group was higher than that in the paraffin group. The efficacy and safety of PEG were reported to be higher than those of paraffin (20), which is completely consistent with the result of the present study, except that in the current study, fig syrup was given instead of paraffin. Similarly, Jordan-Ely et al (21) and McGraw (22) demonstrated the positive effect of PEG and its therapeutic success in treating constipation in children, which corroborates with the results of the current study.

Most physicians attempt to prevent drug dependence and achieve better efficacy of treatment for chronic constipation by prescribing osmotic laxatives such as PEG, which prevents the dehydration of intestinal contents, improves stool consistency, and increases stool

volume. Additionally, PEG facilitates bowel movement by increasing the amount of fluid and water absorbed in the large intestine. It passes through the entire gastrointestinal tract, including the colon without change and dependence on the state of the intestinal microbial flora (23).

The limitations of our study included a short study period; therefore, elongating the study period in future studies may reveal additional effects on gastrointestinal function. Unfortunately, PEG powder is currently available in Iran's pharmaceutical market, which may not be easy for families to use at the recommended doses. In this study, PEG syrup was prepared using fig syrup base at the studied concentration and represented both acceptance and effectiveness. Hence, it is recommended that pharmaceutical companies in Iran take steps to produce ready-made PEG syrups that can be stored for a long time.

Conclusion

According to the results of the present study, PEG syrup was significantly effective in treating chronic functional constipation in children compared to fig syrup. Because it was more effective on abdominal pain, frequency of painful defecation, difficult defecation, straining during defecation, and fear of defecation. Accordingly, the use of PEG syrup for children is recommended due to its better acceptance in this age group.

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Authors' contributions

KK and NM conceived and designed the study. KK, NM, and KF supervised intervention sessions and data collection. FD participated in the data analysis. KF and MM wrote the first draft of the manuscript. All authors contributed to the writing of the paper, and read and approved the final manuscript.

Conflict of interests

The authors declare that there is no conflict of interests.

Ethical approval

The study protocol was approved by the Vice-chancellor for the Research and Technology of the University and registered in the Iranian Registry of Clinical Trials (IRCT20171030037093N2). This study was conducted by the principles of the Declaration of Helsinki and then its protocol was approved by the Ethics Committee of Shahrekord University of Medical Sciences (IR.SKUMS.REC.1396.243).

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