Comparison of polyethylene glycol powder and polyethylene glycol 40% syrup in treatment of chronic idiopathic constipation in pediatrics

Abstract

Introduction: Constipation is one of the most common gastrointestinal complaints in children that can lead to many complications. The aim of this study was to compare the efficacy of polyethylene glycol powder and polyethylene glycol 40% syrup to treat constipation.

Materials and Methods: This study was a nonrandomized semi-experimental clinical trial. The current study was conducted on 80 patients with constipation, referring to Imam Ali (PBUH) Clinic, Shahrekord randomly assigned to two groups of 40 each. Subjects were children under 15 years old with functional constipation selected by simple sampling since 2015. Group 1 was treated with polyethylene glycol powder and Group 2 was treated with polyethylene glycol 40% syrup for two months. During the treatment, the patients were examined five times with 2-week intervals and their symptoms consisting of defecation frequency, stool consistency, painful defecation, bloody defecation, and stool incontinence were registered in a checklist. Data were analyzed using $SPSS_{24}$.

Results: The comparison of patients' total status before and after intervention shows that two groups were assessed in the weak level in the polyethylene glycol powder group 28(0.70%) cases and syrup group 36(0.90%), while after intervention, polyethylene glycol powder group was assessed in the high level 35(87.5%) cases and syrup group 37(92%) cases and most of patients after intervention promoted from weak and intermediate level before intervention to High level.

Conclusion: The findings indicated similar efficacy and treatment response of the PEG powder and syrup. However, the PEG syrup can be used instead of its powder because of pleasant taste and ease of use.

Key words: Constipation, functional constipation, polyethylene glycol

Introduction

Constipation is a common problem in childhood that hurts children and parents and brings about healthcare costs due to development of certain symptoms such as delayed defecation, difficulty defecating, and fecal incontinence resulting from the formation and retention of dense masses of stool in the rectum. The total prevalence of constipation in childhood varies from 0.7% to 29.6%. Inorganic causes (functional constipation) have been reported to be the most common cause of constipation in children. Some children with functional constipation show fecal incontinence and it is a negative indicator in the treatment of these patients (1-3).

Use of laxatives, change in diet, and consumption of more liquids are some of the non-intrusive approaches to treat constipation in children (4). However, these approaches do not ensure successful treatment. Moreover, polyethylene glycol (PEG) is the most effective laxative with the least amount of side effects that can be used for children in the long term (5-7). Physical dependency due to use of PEG has not yet been reported (8), and the PEG does not cause toxic or systemic effects (9).

PEG is a chemical compound with many molecules that is not metabolized by colon bacteria. PEG 3350 without electrolyte is available as powder. This substance is tasteless and colorless, and can be dissolved in liquids such as drinking water and juice. No colon metabolism is the

PEG's advantage over other laxatives that are fermented in the colon. The efficacy of the PEG 3350 for constipation in children has already been studied (10). It is recommended to start treatment at 1 g/kg dose daily that should be moderated once every three days to reach 1-2 defecations per day. In children with chronic constipation, the mean duration of treatment has been reported 3-30 months. Some studies have reported the recovery rate after 1-year treatment to be 60-90% (11, 12).

When oral PEG is prescribed, it causes hydration of the colon contents, facilitation of intestinal passage, and painless excretion in a linear, dose-dependent manner. Therefore, PEG-based laxatives can act more effectively to excrete completely than rectal drugs. These drugs are used for frequent and short-term treatment of chronic constipation (13, 14, 15, 16). Physical dependency due to use of PEG has not yet been reported, and the PEG does not cause toxic or systemic effects.

Currently, PEG powder should be mixed with a large amount of water to be used for treating functional constipation. However, many children cannot tolerate and use it. PEG syrup is more acceptable to children than its powder because the syrup has a smaller volume. Moreover, parents usually administer the PEG powder to children at inappropriate doses. Besides that, the PEG syrup contains appropriate essence and sweetening substances (sucrose) that cause children to accept it more easily. As well, they can be administered with appropriate and uniform doses of the drug and the parents are less likely to administer it at inappropriate doses (17).

Because no study has yet been conducted to investigate this issue, this study was conducted to compare the efficacy of two therapeutic regimens, i.e. polyethylene glycol powder and polyethylene glycol 40% syrup, so that a more appropriate and tolerable regimen can be selected to treat chronic idiopathic constipation (CIC) in children under 15 years.

Materials and Methods:

This study was a nonrandomized semi-experimental clinical trial. The subjects were patients with functional constipation according to the ROME III, under 15 years referring to the Imam Ali (PBUH) Clinic, Shahrekord in 2015-2016. Sampling was done by simple sampling and samples were obtained based on formula: $z1 - \frac{a}{2} = 1/96)$, $d = \frac{\mu 1 + \mu 2}{\alpha\sqrt{2}}$,

$n = \left(\frac{z1 + \frac{\alpha}{2} + z1 - \beta}{d}\right) 2,\ Z1 - B = 0.84,\ D = 0.05,\ n = 39 \cong 40.$

143 children formed the study population of which 63 children were excluded. Exclusion criteria were: having organic constipation, having anorectal abnormality or history of anorectal surgery, recognizing Rome III criteria catching irritable bowel syndrome, and receiving treatment during 2 weeks before initiation of constipation study. Also, children who had mental retardation or metabolic diseases such as hypothyroidism, having Hirschsprung's disease or spinal anomalies or anorectal pathology, undergoing gastric and intestinal surgery, receiving an effective treatment on gastric system (Cisapride, Erythromycin, Pramide), not following the treatment, not tolerating medication. Inclusion criteria were: A. Children under 4 years old, at least 2 items of following cases for one month: Twice stool or less in each week, once or twice fecal in a week (after skill to go WC), fecal mass found in the patient's rectum, and a history of holding stool. B. Children 4-15 years old, at least 2 items of following cases for 2 months: Twice stool or less in each week, once or twice stool incontinence in a week (after skilling to go WC), stool mass in the patient's rectum, a history of stool in larger diameters, and a history for holding stool.

This project was approved in the ethic committee by number of 1394091. Rec. skums.ir in Shahrekord University of Medical Sciences. Also, a written approval of parents were taken.

Then, necessary explanations about the study procedure were given to the parents. Moreover, the legal guardians of the children completed and signed informed consent form. This study was a single blind nonrandomized semi-experimental clinical trial (only practitioner physician and parents were aware of classifying patients and children were not aware of classifying (powder or syrup group and prescription had not different and prescribed based on tendency of children).

The samples (n: 80) were systematically and randomly assigned to two groups as follows: Group A: PEG powder and group B: PEG 40% syrup. The dose of the drug in both groups was determined as 1 g/kg/day. Group A was recommended to dissolve 70 g of the PEG powder (one pack) in 1 liter of cooled boiled water and make a 0.07 g/ml solution (per the manufacturer's instructions). Treatment with the solution at 1 g/kg/day (approximately 14 ml/kg/day) in divided doses was started. The drug dosage could be changed according to the patient's clinical response.

For group B, a pharmacist dissolved 40 g of PEG powder in 100 ml of distilled water and base syrup and made a syrup at 0.4 g/ml dose (per the manufacturer's instructions). The syrup base did not have any interaction with pharmaceutical substances. Moreover, the formulation of the PEG 40% syrup did not need heating or additives. Treatment of group B was started with the PEG 40% syrup (without electrolyte) at 1 g/kg/day (equal to 2.5 ml/kg/day) divided into doses per day. In this group, the drug dosage could be changed according to the patient's clinical response as well.

The patients in both groups were given similar diet-related recommendations. These recommendations included intake of fatty foods such as fried potato and fast food, banana, cooked carrot, white rice, and dairies such as cheese, yoghurt, ice cream, and milk less frequently. The children were recommended to consume low-fat milk and soybean milk (applicable to children under two years). Due to limiting the use of calcium, we recommended the use of other calcium sources such as orange, parsley, soybean, seeds, and cabbage.

In addition, the patients were advised to use fruits and vegetables such as plums, zucchini, *Cucurbita pepo*, tomato, spinach, apples, grapes, peaches, watermelon, cantaloupe, figs, raisins, and whole-grain high fiber foods like popcorn, whole wheat bread, and cereals. Frequent exercise and going to the toilet after meal were also recommended.

The patients were systematically followed up once every two weeks for two months. In the second visit of follow-up, the efficacy, tolerance, and potential side effects of the drugs were assessed and the decision about the efficacy of the administered dose and reconsideration of the dosage was made with reference to the frequency of defecation, stool consistency, rectal bleeding, painful defecation, and fecal incontinence. The purpose of the treatment was smooth and painless excretion of stool and prevention of fecal accumulation in the rectum. The dosage was set in a manner to reach excretion frequency and stool consistency of interest. Each patient was given a form that included information about age, gender, and weight and a table including excretion frequency per week, painful bowel movement, rectal bleeding, stool consistency, and the frequency of fecal incontinence per month that was completed at examinations of the patients.

Data were analyzed using descriptive statistics included frequency, percent, mean, standard deviation and analytical statistics: t-test, K2, and Fisher exact test. Differences were significant at $P<0.05$.

Results:

Polyethylene glycol powder group (group A) included 18(0.45%) males and 22(0.55%) females; syrup consumed group (Group B) included 27 (0.67.5%) males and 13 (0.32.5%) females.

Mean±standard deviation and range of age in the groups A and B were (72.1± 27.9), (15-130) and (72.3± 31.4), (26-156), respectively. The mean± standard deviation and range of weight in the group A and group B was (20.60.1± 7.51), (8-42) and (19.25± 5.93), (13.5-36), respectively. There was no significant difference in the both groups regarding gender, age, and weight (P>0.05).

There was no a significant relationship between two groups before intervention in all variables including frequency of stool incontinence, stool consistency, fecal incontinence, painful bowel movement, rectal bleeding, and frequency of defecation in a month except patient's total status (P>0.05). The overall assessment of the patient's status in the group A 4 (10%) cases (Polyethylene glycol powder group) were in the weak level (P<0.05) and in the groups B, syrup consumed group was 12 (30%) cases in the intermediate level (Table 1).

Table 1: Frequency and percent of variables under the study before intervention

Variables	Frequency	Polyethylene glycol powder group Frequency(%)	Syrup group Frequency (%)	Total(percent)	P-value
Frequency of defecation	Less than 3	30(75)	37(92.5)	67(93.8)	0.115
	3-5	4(10)	2(5)	6(7.5)	
	6-8	5(12.5)	1(2.5)	6(7.5)	
	More than 8	1(2.5)	0(0)	1(1.2)	
Stool consistency	Very tight	37(92.5)	38(95)	75(9.8)	1.000
	tight	2(5)	2(5)	4(5)	
	horny	1(2.5)	0(0)	1(1.2)	
	loose	-	-	-	
Painful bowel movement	No	9(22.5)	5(12.5)	14(17.5)	0.239
	Yes	31(77.5)	35(87.5)	66(82.5)	
Rectal bleeding	No	31(77.5)	25(62.5)	56(70)	0.143
	Yes	9(22.5)	15(37.5)	24((30)	
Frequency of defecationin one month	More than 8	7(17.5)	8(20)	15(18.8)	0.889
	6-8	0(0)	0(0)	0(0)	
	3-5	1(2.5)	1(2.5)	2(2.5)	
	1-2	0(0)	1(2.5)	1(1.2)	
	-	32(80)	30(75)	62(77.5)	
Overall assessment of patient's status	High	0(0)	0(0)	0(0)	0.025
	Intermediate	12(30)	4(10)	16(20)	
	Weak	28(70)	36(90)	64(80)	

After intervention, there was no significant relationship in the all studied variables in two groups (P>0.05) (Table 2).

Table 2: Frequency and percent of variables under study after intervention

Variables	Frequency	Polyethylene glycol	Syrup group	Total (%)	P-value

		powder group Frequency (%)	Frequency (%)		
Frequency of defecation	Less than 3	0(0)	0 (0)	0(0)	0.696
	3-5	4(10)	3(7.5)	7(8.8)	
	6-8	14(35)	11(27.5)	25(31.2)	
	More than 8	22(55)	26(65)	48(60)	
Stool consistency	Very tight	0(0)	0(0)	0(0)	0.755
	tight	5(12.5)	6(15)	11(13.8)	
	horny	35(87.5)	33(82.5)	68(85)	
	loose	0(0)	1(2.5)	1(1.2)	
Painful bowel movement	No	36(90)	38(95)	74(92.5)	0.675
	Yes	4(10)	2(5)	6(7.5)	
Rectal bleeding	No	40(100)	40(100)	80(100)	-
	Yes	0(0)	0(0)	0((100)	
Frequency of defecation in a month	More than 8	0(0)	0(0)	0(0)	0.423
	6-8	1(2.5)	0(0)	1(1..2)	
	3-5	1(2.5)	0(0)	1(1.2)	
	1-2	2(5)	1(2.5)	3(3.8)	
	-	36(90)	39(97.5)	75(93.8)	
Overall assessment of patient's status	High	35(87.5)	37(92.5)	72(90)	0.712
	Intermediate	4(10)	3(7.5)	7(8.8)	
	Weak	1(2.5)	0(0)	1(1.20)	

The comparison of patients' total status before and after intervention showed that the two groups, the polyethylene glycol powder group 28(0.70%) cases and syrup group 36(0.90%) cases, assessed in the weak level; while after intervention, polyethylene glycol powder and syrup groups assessed in the high level 35(87.5%) cases and syrup group 37(92%) cases, respectively and most of patients after intervention promoted from the weak and intermediate level to the high level (Table 3).

Table 3: The comparison groups before and after of total assessment of patient's status

Assessment of patient's status before intervention	Level	High Frequency(Percent)	Intermediate Frequency(Percent)	Weak Frequency(Percent)	Total
Polyethylene glycol powder group	High	0(0)	0(0)	0(0)	0(0)
	Intermediate	11(91.7)	1(8.3)	0(0)	12(30)
	Weak	24(85.7)	3(10.7)	1(3.6)	28(70)
	Total	35(87.7)	4(10)	1(2.5)	-
Syrup group	High	0(0)	0(0)	0(0)	0(0)
	Intermediate	4(100)	0(0)	0(0)	4(10)

	Weak	33(91.7)	3(8.3)	0(0)	36(90)
	Total	37(92.5)	3(7.5)	0(0)	-

Discussion

PEG-based laxatives can act more effectively to excrete completely than rectal drugs. These drugs are used for frequent and short-term treatment of chronic constipation.

Studies have demonstrated that administration of PEG, lactulose, and psyllium have led to the best outcome and function.

Oral powdered polyethylene glycol at a maintenance dose of 0.78 g/kg/day is safe and effective for patients younger than 18 months. Dose and safety profiles are similar to those reported in older children (18).

Cleveland et al, reported patients treated with 17 g of PEG powder per day for four days. At completion of the treatment, it was observed that PEG could lead to improvement of bowel movements function and also no significant change was seen in CBC, serum biochemicals, and urinalyses (19).

The results in a study show low-volume PEG and sennosides. It is much better tolerated, but it had less efficacy than the standard PEG dose given alone (20).

Klauser et al.'s study conducted on 20 patients with constipation demonstrated that administration with 60 g of PEG confirmed the findings of the previous study (21).

Among the drugs that are prescribed for constipation especially in children, willingness to use syrups (mainly due to their pleasant taste and use of flavors in them) is higher. Studies have reported that the patients especially children were unwilling to use the PEG powder due to its unpleasant taste (22, 23).

Dipalma et al. investigated patients with constipation, concluded that administration with 17 g of PEG per day led to increased bowel movement and soft stool consistency. Besides that, no side effects were seen compared to placebo-administered group. It should be noted that in Dipalma et al.'s study, some patients administered with the PEG were reported to develop diarrhea but the difference from the control group was not statistically significant. All these cases confirmed the efficacy of PEG and that no side effects caused by this drug (24).

Incidence of diarrhea in people under treatment with PEG was 2-40%. Moreover, the administered dose of PEG correlated directly to the severity and acquisition of diarrhea, but discontinuing treatment because of severe diarrhea due to administration of PEG was not reported (25).

Cinca et al. studied the efficacy of PEG 3350+E solution and prucalopride in treatment of constipation, 240 patients were selected and randomly assigned to two groups of treatment. The results demonstrated that PEG 3350+E was at least as effective as and generally better tolerated than prucalopride as a treatment for chronic constipation (26). Aghapour et al. compared the efficacy of PEG and lactulose in treating chronic constipation in children, 128 children were enrolled and randomly assigned to two groups of treatment with PEG and lactulose. In this study, the PEG solution was found to be more effective in treating chronic constipation than lactulose (27).

Saneian and Mostofizadeh compared the efficacy of PEG, magnesium hydroxide, and lactulose on functional constipation. 75 children of 1-6 years of age randomly assigned to three groups of PEG, magnesium hydroxide, and lactulose. The patients were treated for one month with the

standard doses of these drugs. After the treatment, fewer side effects were seen in patients treated with the PEG (28).

This study shows that the PEG powder and syrup are equally effective. However, retention and availability of the PEG powder are much higher than its syrup. Regarding the PEG powder, as with the syrup, no risk or a special complication was reported which is an advantage of this drug.

Limitation of the study

One of the limitations of this study was that complications of drugs were not studied through laboratory tests, and it is suggested to be considered in future studies.

Conclusion

The findings represented similar efficacy of the PEG powder and syrup on frequency of defecation, fecal consistency, painful bowel movement, rectal bleeding, and fecal incontinence in the two groups. However, retention and availability of the PEG powder are easier than its syrup. Moreover, the patients are more willing to take the PEG syrup rather than the PEG powder because of its more pleasant taste, which is a remarkable advantage of the PEG powder.

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