

Comparing the efficacy of polyethylene glycol (PEG), magnesium hydroxide and lactulose in treatment of functional constipation in children

Hossein Saneian¹, Neda Mostofizadeh²

¹ Assistant Professor, Department of Pediatrics, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.

² Resident, Department of Pediatrics, School of Medicine And Student Research Committee, Isfahan University of Medical Sciences, Isfahan, Iran

BACKGROUND: Constipation is one of the common problems in childhood and consists of 3% of referrals to pediatricians and 25% of pediatric gastroenterologists. Aperients are common alternatives for treating chronic constipation. The present study aimed to compare the efficacy of three laxatives [polyethylene glycol (PEG), magnesium hydroxide, and lactulose]. **METHODS:** In this randomized clinical trial, 1 to 6 year old children with functional chronic constipation (the patients had functional chronic constipation based on ROME III criteria) were studied. 75 patients were divided into three 25 member groups through randomization method. The patients of each group received either of the polyethylene glycol, magnesium hydroxide, or lactulose medications in a standard dosage. After a month, the results were assessed and analyzed through statistical tests. **RESULTS:** Comparing the frequency of increased defecation in patients of the three groups also found no significant difference among them; however, mean increase of defecation frequency was higher in the magnesium hydroxide group. Compared to patients who had more than three times of defecation per week, PEG group was significantly higher than the other two groups ($p < 0.05$). Comparing the side effects showed that the prevalence of side effects was lower in the polyethylene glycol group than the other two groups. The patients had a significantly higher satisfaction from the taste of polyethylene glycol and lactulose ($p < 0.01$). **CONCLUSIONS:** Although the total mean of increase in defecation frequency after the treatment was higher in the magnesium hydroxide group, the indicator of defecation frequency greater than three times per week was higher in the polyethylene glycol group which indicated the success of treatment in this group. In total, comparing the therapeutic results and satisfaction of the patients, it can be concluded that polyethylene glycol can be used as one of the best alternatives to treat constipation.

KEYWORDS: Constipation, Polyethylene Glycol, Magnesium Hydroxide and Lactulose, Laxatives

BACKGROUND

Constipation is one of the common issues among children and also the cause of 3 percent of referrals to pediatricians.^[1] The actual incidence of constipation estimated between 1 to 30 percent.^[1] The highest prevalence of constipation reported in preschool aged children.^[1]

According to definition, if the frequency of defecations is less than twice a week or it is done once every three days while painful, it is considered as constipation.^[2] Clinical manifestations of constipation include a wide range of items such as irregular bowel movement, small and hard stool, painful stool excretion with large diameter and fecal incontinence (encopresis; volitional or non-volitional feces excretion).^[3,4] The main causes of constipation in children divided into functional and organic categories.^[5] In more than 95 percent of the cases, functional constipation is the cause of constipation in

children.^[6] According to diagnostic indicators of ROME III which has been defined by multinational working teams to develop diagnostic criteria for functional disorders,^[7,8] the prove of functional constipation has been two cases out of 6 descriptive indicators (frequency of defecations, hardness, incontinence or retentive posturing) which should be observed one month in infants or two months in children (Table 1). For treatment of functional chronic constipation; based on the intensity of constipation in growth stage,^[9] which usually is a detailed program, use of laxatives, behavioral changes, nutritional modifications and accurate follow-up is necessary.^[10] The used laxatives are polyethylene glycol (PEG), magnesium hydroxide, lactulose and mineral oils.^[11]

Various studies have been done so far reviewing the efficacy of laxatives to treat functional constipation which mainly have compared the two drugs to each other.^[12-15] In this study, we intent to determine

Address for correspondence: Hossein Saneian, Assistant Professor, Department of Pediatrics, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran. E-mail: saneian@med.mui.ac.ir

Received: 28-12-2011; **Revised:** 5-02-2012; **Accepted:** 21-02-2012

Table 1. Indicators of diagnosis the functional constipation in children^[8]

Rome III criteria for the diagnosis of functional constipation in children	
Infants and Toddlers	Children with developmental age 4 to 18 years
<i>At least two of the following present for at least one month</i>	<i>At least two of the following present for at least two months</i>
Two or fewer defecations per week	Two or fewer defecations per week
At least one episode of incontinence after the acquisition of toileting skills	At least one episode of fecal incontinence per week
History of excessive stool retention	History of retentive posturing or excessive volitional stool retention
History of painful or hard bowel movement	History of painful or hard bowel movement
Presence of a large feces mass in the rectum	Presence of a large feces mass in the rectum
History of large-diameter stool which may obstruct the toilet	History of large-diameter stool which may obstruct the toilet

the advantages and disadvantages of polyethylene glycol (PEG), magnesium hydroxide and lactulose on treatment of functional constipation in children through a comparative review. The results can be used to develop an appropriate protocol for treatment of functional constipation in children.

METHODS

In this prospective clinical trial, 1 to 6-year-old children with functional chronic constipation were studied who referred to Pediatric Clinic of Amin Hospital, Isfahan during a year.

The children could be enrolled in the study provided they had pebble like and hard stool or hard bowel movement twice a week or more along with no evidence of any structural, endocrine and metabolic diseases for two months.

Moreover, they could be excluded from the study provided that they had any organic suspected symptoms (fever, vomiting, urinary incontinence, diarrhea, growth disorder, anal stenosis, unexplained bleeding with fisher and/or an abnormal point in examination such as abnormal DTR during the treatment), having known cardiac, pulmonary, neurological and renal diseases and anorectal malformation during the treatment, having any disease causes children's treatment course not to be improved, loss of follow-up and also changing disease diagnosis and/or treatment withdrawal.

The sample size calculated 75 subjects divided in three 25-subject groups by systematic randomization using the randomization software. After obtaining the patients' history and full clinical examination (such as rectum examination) by pediatric resident, they entered the study provided not to have suspected symptoms (fever, vomiting, urinary incontinence, diarrhea, growth disorder, anal stenosis, bleeding and etc). Besides, systematic randomized sampling method was

used for sample allocation in each of the three groups.

It should be noted that ethically none of the patients received placebo. Moreover, in terms of hard fecal impaction, first the fecal impaction evacuated outpatient or admitted with edible paraffin enema and also saline enema (3 nights edible paraffin enema and 3 nights saline enema).

The intervention conducted in four stages as the following:

1. Verbal education and pamphlet by pediatric resident
2. Diet (prepared list)
3. Laxatives for a month and disimpaction, if necessary.
4. Patients follow-up (a week later and then monthly for 4-6 month The four mentioned staged conducted for all the patients and the difference was only in laxative they received.

The first group received lactose (Tolid Daroo, Tehran, Iran) 1 cc/kg/day (augmentable to 3 cc/kg/day and its report, if any). The second group received magnesium hydroxide (Tolid Daroo, Tehran, Iran) 1 cc /kg/day (augmentable to 3 cc/kg/day and its report, if any) and the third group received polyethylene glycol with no electrolyte 40% (School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran) 1 cc /kg/day (augmentable to 3 cc/kg/day and its report, if any).

Therapeutic result was evaluated as defecation equal or more than 3 times a week without pain and bleeding (smooth, relax and large-diameter) in addition with fecal incontinence less than twice a month at the end of one month treatment.

The data were analyzed through non-parametric tests as chi-square, ANOVA, and Mann-Whitney pare the efficacy of the three used drugs. Software SPSS version 15 was used for statistical analysis.

RESULTS

Comparing the demographic indicators of the study subjects are illustrated in table 2. As indicated, the study subjects had no difference in terms of age, weight, height and also in terms of constipation onset age, frequency of defecation and duration of constipation. In terms of sex also the number of boys and girls in the three groups showed no significant difference together ($p < 0.05$).

After passing the treatment course, the mean increase of defecation frequency in magnesium hydroxide (4.67 ± 2.29) was significantly lower than PEG (3.56 ± 1.99) and lactulose (3.16 ± 1.72) ($P = 0.015$); however, comparing the mean increase of defecation frequency among the three groups and according to division showed an increase which significantly there was no difference between the three groups (Table 3) ($p = 0.100$).

However, statistical analysis showed that the number of those had defecation more than three times a week was significantly more in PEG group than two

other groups ($p = 0.040$).

The clinical examination before the study showed that the frequency of fecal impaction in PEG group was 10 subjects (33.3%), in magnesium hydroxide group was 5 subjects (16.7%) and in lactulose group was 8 subjects (26.7%). In this regard, there was no significant difference between the three groups before the study ($P = 0.334$).

However, after the study, the frequency of this case among the PEG group was zero, in magnesium hydroxide group was 1 subjects (3.3%) and in lactulose group also was 5 subjects (16.7%) which statistically showed a significant reduction in first ($p = 0.023$) and second group ($p = 0.027$) and also no significant reduction was seen in the lactulose group ($p = 0.123$).

The reported side effects after drug consumption are shown in table 4. The statistical studies showed that incidence of abdominal pain in PEG significantly was lower than other groups ($p = 0.001$). Furthermore, the incidence of bloat in PEG and magnesium hydroxide groups was significantly lower than lactulose group ($p < 0.001$).

Table 2. Comparing the demographic characteristics and disease of the study subjects

Variables	Polyethylene glycol		Magnesium hydroxide		Lactulose		P-value
	Mean	SD	Mean	SD	Mean	SD	
Age (years)	3.26	1.50	3.11	1.06	3.19	1.36	0.904
Weight (kg)	16.13	13.70	14.01	2.11	13.93	3.76	0.511
Height (cm)	91.57	18.14	95.33	8.43	94.06	11.04	0.535
Constipation onset age (months)	18.33	9.55	21.06	11.01	17.63	11.89	0.436
Frequency of defecation(/week)	1.33	1.18	1.37	2.44	1.53	1.43	0.896
Duration of suffering (months)	20.86	13.26	16.29	11.36	20.64	14.14	0.301

Table 3. Comparing the increase of defecation frequency among the three groups in terms of division

GROUPS	TIME	Less than 3 times a week	3-5 times a week	6-8 times a week	More than 8 times a week
		Number (%)	Number (%)	Number (%)	Number (%)
Polyethylene glycol		4 (13)	12 (40)	13 (44)	1 (3.3)
Magnesium hydroxide		3 (10)	4 (13)	16 (54)	7 (23)
Lactulose		6 (20)	12 (40)	10 (33)	2 (7)

P = 0.100

Table 4. Comparing the prevalence of pharmacological side effects in the studied groups

Side effects	Polyethylene glycol		Magnesium hydroxide		Lactulose		P-value
	Number		Number	Percentage	Number	Percentage	
Abdominal pain	2 (7)		17	57	14	47	0.001
Nausea and vomiting	0 (0)		0	0	1	3	0.221
Bloat	2 (7)		1	3	17	57	< 0.001
Diarrhea	0 (0)		5	17	1	3	0.024
Irritation around stomach	1 (3)		1	3	2	7	0.533

The results presented as number (%).

Furthermore, magnesium hydroxide significantly caused more diarrhea than other two drugs ($p = 0.024$). The satisfaction rate of children from taste of drugs in lactulose (76.7%) and PEG (73.3%) significantly was higher than magnesium hydroxide (40.00%) ($p = 0.005$). However, in terms of parents' satisfaction rate from the therapeutic results, successful and partly successful comments in PEG (90%) and magnesium hydroxide (97%) groups significantly was higher than lactulose group (83%) ($p = 0.48$).

Four subjects in PEG (13.3%) and 5 subjects in magnesium hydroxide group (16.7%) and also 10 subjects in lactulose group (23.3%) were forced to change the drug. Although this amount was less in PEG group than other groups, there was no significant difference between the three groups ($p = 0.129$).

DISCUSSION

The present study conducted aiming to compare the efficacy of three polyethylene glycol (PEG), magnesium hydroxide and lactulose drugs to treat functional constipation in children; and the results showed that although every three drugs increased defecation frequency in patients, these findings have been confirmed in other previous studies.^[12-15]

Crude comparison of mean increase in defecation frequency between the three groups indicated a significant reduction in magnesium hydroxide than other two groups. However, with separating the number of defecation and comparison based on frequency of the study subjects in each category indicated that there was no significant difference among the three groups in this regard.

Nevertheless, other aspects for selecting an appropriate medication to treat chronic constipation in children also should be taken into account. Because studies have shown that one of the major causes of failure in constipation treatment is early drug withdrawal or lack of appropriate cooperation by patients.^[13-15] Therefore, evaluating the pharmacological side effects is necessary to increase therapeutic efficacy and patients' satisfaction.

In the present study, the studied side effects of PEG generally were lower than other two drugs. And reduction of abdominal pain and bloat significantly was better by this drug than those other two. This finding was in accordance with other previous studies.^[13-15]

Among the three studied drugs, magnesium hydroxide significantly caused more diarrhea among the consumers; probably that is why mean defecation frequency in magnesium hydroxide users was higher than two other drugs. The point that the diarrhea frequency was higher in these patients devalued the higher level of defecation frequency.

Preanal, abdominal pain during defecation, bleeding during defecation and anus pain during defecation among the three groups had no difference after therapeutic measures and every three drugs similarly (statistically) reduced bleeding, abdominal pain and rectal pain (all the patients had defecation pain at the beginning of the study). In this study, according to the standard criteria and previous studies, the determinant indicator of treatment success was considered three times or more defecation per week along with at least one soiling in two weeks.

The results showed that the patients who had more than three defecations per week, it was more in PEG group than two other groups.

Therefore, although total mean increase in defecation frequency after the treatment was higher in magnesium hydroxide, the indicator of defecation frequency more than three times per week which indicates treatment success was reported higher in PEG group. The study of Vo Voskuil et al also indicated the 2-fold treatment success of PEG than lactulose.^[14] However, parents of patients were significantly more satisfied from therapeutic results of PEG and magnesium hydroxide than lactulose which this finding confirmed the above mentioned points.

After the treatment course, due to treatment failure or not achieving to the therapeutic goals, some of patients forced to change their drug or increase other drugs. Although the difference between the three groups statistically was not significant, the amount of drug change was lower in PEG than other two drugs.

In this study, the prevalence of fecal impaction in rectum was similar among the three groups before the treatment. After the treatment, although the prevalence of fecal impaction in rectum reduced in every three groups, the amount was significantly lower in PEG and magnesium hydroxide groups than lactulose. The study of Dupont et al indicated that lower fecal impaction in rectum was along with consumption of PEG rather than lactulose.^[13]

The acceptance rate of children and their satisfaction from drug's taste in PEG and lactulose significantly was higher than magnesium hydroxide. In the study of Loening-Baucke and Pashankar the acceptance rate of PEG also reported higher than magnesium hydroxide.^[15]

CONCLUSIONS

Generally, comparing the therapeutic results, side effects and satisfactory rate of patients in this study showed that due to lack of serious side effects, PEG (polyethylene glycol) can be used as the first pharmacological alternative to treat functional constipation in children.

ACKNOWLEDGMENTS

This paper is derived from a specialty thesis No. 387194 in Isfahan University of Medical Sciences.

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How to cite this article: Saneian H, Mostofizadeh N. Comparing the efficacy of polyethylene glycol (PEG), magnesium hydroxide and lactulose in treatment of functional constipation in children. *J Res Med Sci* 2012; 17(Special 1): S145-S149.

Source of Support: Isfahan University of Medical Sciences, **Conflict of Interest:** None declared.