

# Comparative Evaluation between the LaxaPlus Barij® and Polyethylene Glycol (4000) in the Pediatric Functional Constipation in Children 2–15 Years Old

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## INTRODUCTION

Constipation is a common problem in children, and it is estimated that between 1% and 33% of children have constipation.<sup>[1]</sup> A child with constipation has fewer bowel movements than average. In these cases, the passage of feces in the intestine is complicated and is accompanied by pain. Most of the children with constipation do not have the medical problem that causes constipation.<sup>[2]</sup>

Oral laxatives and regular toilet training are the primary treatments. Osmotic laxatives increase fluid volume in the stool by improving the movement of stool in the colon and improving excretion. Osmotic laxatives include polyethylene glycol (PEG), which is used as the first line of treatment in pediatric constipation. In a 4-week

## ABSTRACT

**Objective:** This study aimed to compare the LaxaPlus Barij® and polyethylene glycol (4000) in pediatric (children 2–15 years old) functional constipation.

**Methods:** The present study is a randomized clinical trial. The study population included patients with functional constipation aged 2–15 years who were referred to the gastrointestinal clinic of Imam Hossein hospital in Isfahan in 2019. Patients were randomly assigned into two treatment groups. Data analysis was performed using SPSS software. The significance level in the present study is considered  $<0.05$ .

**Findings:** Sixty children with functional constipation were selected based on the inclusion and exclusion criteria in this study. The present study results showed no significant difference between demographic characteristics, including age, weight, and gender of children with constipation in the two groups ( $P > 0.05$ ). The present study results showed that both groups' mean stool consistency and the number of bowel movements increased significantly after the intervention ( $P < 0.05$ ). However, the number of bowel movements in the first group was significantly higher than in the second group ( $P < 0.05$ ). **Conclusion:** The present study results showed that both drugs effectively treat children with functional constipation. However, after 8 weeks of intervention, the frequency of bowel movements, pain intensity, and abdominal pain in the group LaxaPlus Barij® was more effective. However, the level of satisfaction did not differ significantly between the two groups.

**KEYWORDS:** Child, constipation, LaxaPlus Barij®, polyethylene glycol

study of children aged 1–18 years, PEG powder was given to children at a dose of 0.7 g/kg, which improved constipation and fecal incontinence.<sup>[3-5]</sup>

In traditional Iranian medicine, herbs are used to treat constipation. In a case-control clinical study examining the efficacy and safety of the jujube fruit extract for the treatment of constipation of unknown origin, 37 patients with constipation received 18 jujube extracts and 19 placebos. Two in the case group and 16 in the control group dropped out of the study due to severe constipation. This

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study showed that intestinal transit time was significantly reduced in the case group at 11 weeks. The severity of symptoms was reduced from 6 to 2 in the case group and 5 in the control group. Quality of life scores improved in both groups, and the study found that alcohol is effective and safe.<sup>[6]</sup> In another study on roses, the frequency of defecation increased, and the consistency of stool decreased but had no effect on intestinal transit time.<sup>[7,8]</sup>

In a case–control study performed on two groups of mice, the case group received a violet flower extract, and the control group received bisacodyl. Thirty minutes later, charcoal was given to both groups. The ratio of the length of the path charcoal had traveled in the intestine to the total length of the intestine in both groups was evaluated. The results showed the effectiveness of violet flower extract in intestinal transit.<sup>[9]</sup> Fruit seeds, also known as seeds, effectively treat constipation in a review article. The effect of other medicinal plants, such as asparagus, borage, and Sapistan seeds has been confirmed in other studies as laxative plants in the treatment of constipation.<sup>[10-17]</sup> LaxaPlus Barij® Syrup is an herbal medicine used to treat constipation. This syrup is prepared from the extract of jujube, rose, asparagus, violet flower, borage, quince seeds, and *Cordia myxa* fruit, which is used in traditional Iranian medicine. Despite the mucilage-polysaccharide compounds, it shows desirable and safe laxative effects. Although LaxaPlus Barij® syrup is the only approved and available herbal medicine for children in Iran, no published clinical trial study has supported this drug's effectiveness. Here, we decided to investigate the effect of this drug on pediatric constipation.

## METHODS

The present study was a randomized clinical trial. The study population included patients with functional constipation aged 2–15 years who were referred to the gastrointestinal clinic of Imam Hossein hospital in Isfahan in 2019. Inclusion criteria include the children with functional constipation, whose constipation was confirmed by the Rome IV criteria, age between 2 and 15 years, and parental consent. Furthermore, exclusion criteria in this study were causing intolerable side effects of the drug or if the patients took any medication for 2 weeks before the study. The present study protocol has been approved by the Ethics Committee of Esfahan University of Medical Sciences (IR.MUI.MED.REC.1399.082) and the clinical trial code “IRCT20190410043224N3.”

A medical resident identified eligible individuals and then randomly assigned them into two groups.

In this clinical trial, 60 children with functional constipation were selected according to the inclusion and

exclusion criteria. The demographic characteristics of patients (age, sex, ethnicity, and race) in both groups were recorded. Patients in the control group were given PEG powder at a dose of 1–1.5 g/kg for 3 days to cleanse the intestines.

At the beginning of the intervention, a clinical examination was performed by examining the perineal area in all children to determine the cause of constipation. During the first visit, seven questions and critical points were asked: frequency of defecation, stool consistency (Bristol stool scale), pain during defecation, retention and incontinence of stool, abdominal pain, absenteeism from school, and side effects, such as diarrhea and heartburn.

The patients were divided into two arms of intervention and control groups, which were as follows:

In intervention group, LaxaPlus Barij® was administered as 1 mL/kg daily divided into three doses in children with bodyweight <30 kg, and 10 mL three times daily in children with bodyweight more than 30 kg orally, half an hour before meals for 8 weeks.

In control group: PEG (4000) Powder (Sepidaj Pharmaceutical Company) was administered as 0.7 g/kg, orally three times daily for 8 weeks.

Data analysis was performed using SPSS software, version 16 (Computer Associates International Inc.; IBM Corporation; Microsoft Corporation; Based in Chicago). The normality of the distribution for the data was checked using the Kolmogorov–Smirnov test. Quantitative data are reported as mean and standard deviation, and qualitative data are reported as percentages and frequency. Chi-square, independent *t*-test, and analysis of variance were used to compare the data. The statistical significance level in the present study is considered <0.05.

## RESULTS

A total of 126 eligible patients were recruited for the study. Six children were excluded during the study due to meeting the exclusion criteria. In the present study, 120 children with functional constipation participated in the whole study to the end, with 60 patients in each study group. The first group included 60 patients who have received medication LaxaPlus Barij® and the second group included 60 patients who have received PEG [Figure 1]. Table 1 compares the demographic characteristics of the studied patients in the two groups. As shown in Table 1, no significant difference was observed between demographic characteristics, including age, weight, and gender in sick children in the two groups ( $P > 0.05$ )

Table 2 also examines the stool consistency, frequency of bowel movements, and pain intensity before and after

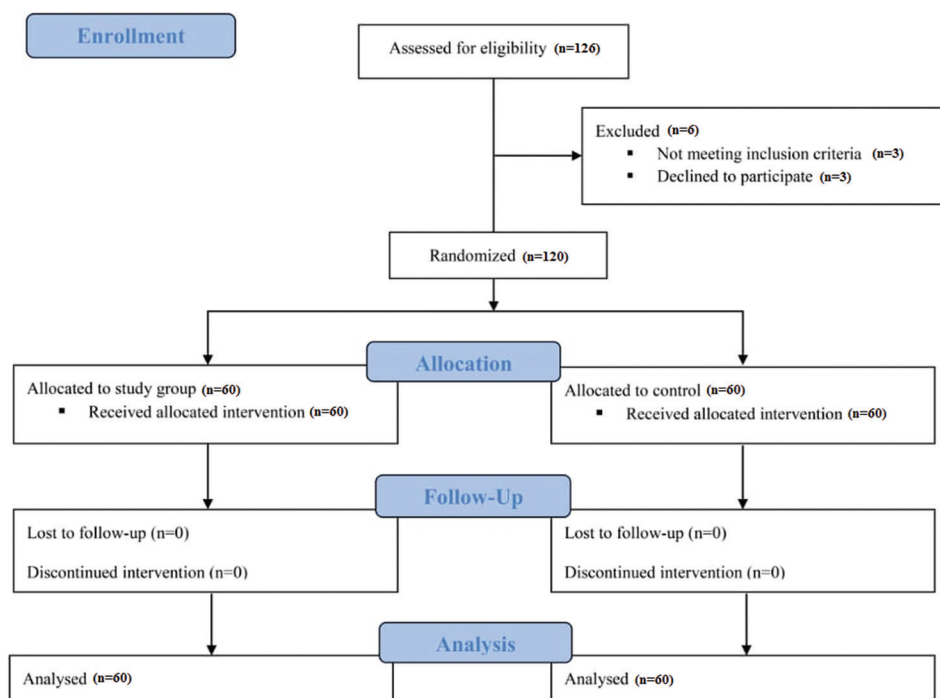


Figure 1: Flowchart of participants overview of this study

Table 1: Comparison of patients' demographic characteristics in two groups

Variable	LaxaPlus Barij®	Polyethylene glycol	P
Age (years)	1.95±4.6	2.37±5.454	0.26*
Weight (kg)	5.8±18.35	6.05±20.18	0.11*
Gender (%)			
Girl	35 (58)	31 (52)	0.30**
Boy	25 (42)	29 (48)	

\*Independent t-test, \*\*Chi-square test

the treatment intervention in the study groups. Based on the results, the mean stool consistency and the number of bowel movements in both groups increased significantly after the intervention ( $P < 0.05$ ). However, the number of bowel movements in the first group was significantly higher than in the second group ( $P < 0.05$ ). The mean pain intensity in both groups decreased significantly after the intervention, significantly lower in the first group ( $P < 0.05$ ). Furthermore, the results related to the satisfaction of both treatment groups show that despite more satisfaction in the first group, no significant difference was observed between the average satisfaction in the two groups ( $P > 0.05$ ).

Table 3 compares pain during defecation, fecal incontinence, and abdominal pain before and after the intervention in the two groups. According to the results, both treatment groups effectively reduced abdominal pain, pain during defecation, and fecal incontinence ( $P < 0.05$ ). Furthermore, according to the results, abdominal pain and pain during defecation

in the first group had a greater reduction than the second group ( $P < 0.05$ ).

## DISCUSSION

Constipation in children is a common problem. A constipated child has infrequent bowel movements or hard, dry stools. Common causes include early toilet training and change in diet. Fortunately, most of the cases of constipation in children are temporary. Therefore, the purpose of this study was to compare the evaluation between the LaxaPlus Barij® and PEG (4000) in pediatric functional constipation in children 2–15 years old.

There was no significant difference between demographic characteristics, including age, weight, and gender of children with constipation in the two groups. Therefore, any effect on the main variables in the groups was attributable to the impact of therapeutic intervention.

In general, the present study results showed that the mean stool consistency and number of bowel movements in both groups increased significantly after the intervention. However, the number of bowel movements in the first group was significantly higher than in the second group. The mean pain intensity in both groups decreased significantly after the intervention, significantly reduced in the first group. Furthermore, the results related to the satisfaction of both treatment groups show that despite more satisfaction in the first group, no significant difference was observed between the average satisfaction

in the two groups. In both treatment groups, abdominal pain, pain during defecation, and reduction of fecal incontinence were influential and significant. Furthermore, according to the results, abdominal pain and pain during defecation in the first group had a more significant reduction than in the second group.

In a similar study, Saneian *et al.* conducted the effect of a herbal-based Laxative (Goleghand®) and PEG on functional constipation among children in a randomized controlled trial. According to the results of this study, 60 patients have been enrolled in the study. Parental satisfaction scores did not change significantly in either group or over the follow-up period. The results showed that the effect of time ( $P < 0.001$ ) and also the impact of group type ( $P = 0.01$ ) on the number of fecal defecations was significant. The mean number of defecations increased first and then decreased significantly over time, but this decrease was more effective in the PEG group

**Table 2: Comparison of fecal consistency, number of defecation, pain intensity, and satisfaction before and after the intervention in the two groups**

Variable	LaxaPlus Barij®	Polyethylene glycol	P*
Stool consistency			
Before intervention	0.67±1.5	0.50±1.7	0.23
After the intervention	0.77±3.4	0.56±2.7	0.06
P**	0.01	0.04	-
Number of defecations			
Before intervention	1.69±3.5	1.2±3.1	0.81
After the intervention	3.9±7.3	3.4±5.5	0.02
P**	0.001	0.001	-
Intensity of pain			
Before intervention	2.30±4.8	2.60±5.1	0.32
After the intervention	0.07±0.65	0.33±1.42	0.01
P	0.001	0.001	-
Satisfaction rate	0.77±2.64	0.80±2.16	0.07

\*Independent *t*-test, \*\*Paired *t*-test

than in the Goleghand® group ( $P = 0.001$ ). Furthermore, the effect of time on the fecal consistency score was substantial ( $P = 0.047$ ). The mean score of fecal consistency in both groups decreased over time. These results are consistent with the findings of the present study. Finally, the authors of this study concluded that Goleghand® was similar in efficacy to PEG for 8 weeks of pediatric functional constipation treatment in this randomized clinical trial. Goleghand® can be considered a new herbal laxative drug for pediatric functional constipation.<sup>[18]</sup>

Literature reviews showed that PEG was compared with placebo or other laxatives, including lactulose, milk of magnesia, and liquid paraffin. As the PEG is proposed as a first-line drug in functional constipation, it was chosen as standard therapy for our study's control group. Our follow-up duration was 8 weeks, an acceptable period based on similar studies conducted from 2 weeks to 12 months. A double-blind, multicenter, placebo-controlled trial assessed the efficacy of three different doses of PEG 3350 in 103 children with idiopathic functional constipation showed that all doses resulted in significantly higher rates of treatment success. Another study also revealed that the efficient daily dose of PEG 4000 was approximately 0.5g/kg/day in >90% of children with constipation.<sup>[19-30]</sup>

In conclusion, the results of the present study showed that both drugs are effective in treating children with functional constipation. However, after 8 weeks of intervention, the frequency of bowel movements, pain intensity, and abdominal pain in the group LaxaPlus Barij® was more effective. However, the level of satisfaction did not differ significantly between the two groups.

## AUTHORS' CONTRIBUTION

P. Nasri, S. Saeidi and M. Khademian have contributed

**Table 3: Comparison of presence of pain during defecation, having fecal incontinence, and having abdominal pain before and after the intervention in the two groups**

Variable	LaxaPlus Barij® (%)	Polyethylene glycol (%)	P*
Existence of pain during defecation			
Before intervention	24 (40)	26 (43)	0.4
After the intervention	15 (25)	19 (31)	0.04
P**	0.001	0.01	-
Having fecal incontinence			
Before intervention	18 (30)	17 (28)	0.9
After the intervention	7 (12)	11 (18)	0.08
P**	0.001	0.04	-
Having abdominal pain			
Before intervention	48 (80)	51 (85)	0.12
After the intervention	20 (34)	29 (48)	0.01
P**	0.001	0.001	-

\*Independent *t*-test, \*\*Paired *t*-test

to the concept and design. H. Saneian, F. Famouri, S. Sadeghi, L. Mohammad Taghizadeh Kashani have contributed to the definition of intellectual content and literature search. S. Saeidi and P. Nasri contributed to the data analysis. P. Nasri, S. Saeidi and M. Khademian contributed to the manuscript preparation; and all authors edited the final version of the manuscript.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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