International Journal of Basic & Clinical Pharmacology
Shinghal U et al. Int J Basic Clin Pharmacol. 2023 Jul;12(4):551-555
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20231890

Original Research Article

Comparative efficacy of polyethylene glycol 3350 monotherapy against polyethylene glycol 3350 plus sodium picosulfate combined therapy in treating fecal impaction in pediatric functional constipation patients

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Received: 26 April 2023
Accepted: 24 May 2023

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ABSTRACT

Background: Functional constipation (FC) is a common pediatric problem worldwide. The management of FC comprises of a short initial disimpaction phase followed by long-term maintenance phase. Currently, polyethylene glycol (PEG) is considered as standard disimpaction therapy in pediatric FC patients. The aim of our study was to compare the efficacy of polyethylene glycol 3350 monotherapy with polyethylene glycol 3350 and sodium picosulfate combined therapy in treating fecal impaction in pediatric FC patients.
Methods: All children (aged >1 year) diagnosed with FC as per ROME IV criteria and presenting to the out-patient department of pediatric gastroenterology, hepatology and nutrition unit of a tertiary health centre in north Indian Himalayan state were randomized into two open label, prospective, parallel groups, namely group A (receiving PEG 3350 monotherapy) and group B (receiving combined PEG 3350 plus sodium picosulfate therapy), over a period of 13 months. The outcome was evaluated as successful disimpaction with onset of loose/watery stools (Type-7 of Bristol stool chart scale). The success rates and mean time to disimpaction for two groups were computed and compared.
Results: Eighty-one patients were randomized into two groups. The mean time to disimpaction was found to be significantly lower ($p<0.001$) for group B (2.37±1.16 days) when compared to group A (4.00±1.43 days). There was successful resolution of impaction in both groups. No adverse events were reported in either group.
Conclusions: Combined PEG 3350 and sodium picosulfate therapy significantly reduces the disimpaction time when compared with PEG 3350 monotherapy in pediatric population, however both the therapies appear similar in achieving successful disimpaction.

Keywords: Bristol stool scale, Disimpaction, Functional constipation, Polyethylene glycol, ROME IV criteria, Sodium picosulfate

INTRODUCTION

Functional constipation (FC) is a frequently encountered childhood problem comprising nearly 25% of the pediatric gastroenterology OPD, and pooled prevalence of around 9.5%.[1,2] In India, the prevalence ranges from 0.5% to 30.8%.[3,4] The pediatric constipation may be caused by several underlying disorders (for example, Hirschsprung's disease, gluten enteropathy, hypothyroidism, etc.) but no underlying cause can be identified in >90% children presenting with constipation, such children are said to have FC.[5]

The FC patient, according to ROME IV criteria, must have 2 or more of the following symptoms occurring at least 1/week for a minimum of 1 month: ≤2 defecations in the toilet per week in a child of at least 4 years of age, ≥1 episode of fecal incontinence per week, history of retentive

posturing, history of painful/hard bowel movements, presence of a large fecal mass in the rectum and history of large stools that obstruct the toilet.[6]

The most common underlying event that predisposes to FC is the avoidance of defecation due to social reasons like travelling or while in school. This leads to build-up of feces in colon and more and more resorption of water from the feces by the colonic mucosa, as a result the retained fecal material becomes harder and cause pain on evacuation. This pain on evacuation further promotes the withholding of stools and the rectum becomes progressively distended leading to fecal incontinence and reduced GI motility causing anorexia and abdominal distension.[6]

The management of pediatric FC includes patient and parents counselling, toilet training, dietary modifications, drug therapy and follow-up.[7] The drug therapy consists of two phases, an initial disimpaction phase followed by a prolonged maintenance phase. Disimpaction means dislodging the hard, impacted feces from the rectum. Successful disimpaction is must before initiating the maintenance therapy. Currently, most of the pediatric gastroenterology centres are treating fecal impaction on an inpatient basis using high dose oral polyethylene glycol (PEG) for 1-3 days.[8] But there are three major concerns: firstly, inpatient management is associated with higher health care costs; secondly, poor compliance of patients for such high dose of oral PEG, thereby requiring nasogastric administration of PEG and; thirdly, response rates are not as satisfactory as expected.

Thus, taking these issues into consideration, our study was designed to determine any additional advantage of adding stimulant laxative (sodium picosulfate) to PEG over PEG alone in resolution of pediatric fecal impaction on an out-patient basis while PEG is currently the most commonly used agent for treatment of fecal impaction.

METHODS

The study was an open label, prospective, parallel group randomized controlled clinical trial conducted in the out-patient department of pediatric gastroenterology, hepatology and nutrition unit of a tertiary health centre in Himalayan region (Shimla, Himachal Pradesh) in India from 9th July 2021 to 16th August 2022. All patients in the age group of 1-18 years fulfilling the Rome IV criteria of functional constipation were included in the study except those presenting with red flag signs of constipation which include constipation starting before 1 month of age, passage of meconium after 48 hours, failure to thrive, gluten enteropathy, family history of Hirschsprung disease, thyroid disorders, ribbon stools, bloody stools, severe distension of abdomen, fever, bilious vomiting, perianal fistula, absent anal/cremasteric reflex, abnormal position of anus, anal scars, tuft of hair on spine, sacral dimple.[9]

Sample size

Efficacy of polyethylene glycol 3350 is 56% as per the study by Voskuijl et al in FC in pediatric age group and we assume 30% (effect size) absolute improvement for those on study therapy (i.e., 86% of the subjects will have a successful outcome).[10]

For a two-sided test of 5%- Formula for calculating sample size was

$$Size\ per\ group = C \times \frac{\pi_1\ (1 - \pi_1)\ +\ \pi_2\ (1 - \pi_2)}{(\pi_1\ -\ \pi_2)^2}$$

Where C= 10.5 for 90% power.

π_1 and π_2 are proportion estimates. Here π_1=0.56 and π_2=0.86

So, the sample size calculated was 36.68 × 2, i.e., 37 × 2 = 74

With 10% drop rate, the sample size was 81.

The enrolled patients were randomized into two groups (group A and group B) at the first OPD visit. The randomization was based on random numbers generated by a computer-based technique. These numbers were placed in an opaque sealed envelope. These sequentially numbered envelopes were provided by a blinded co-author (P. K. Kaundal), who had no access to study subjects. The study subjects in group A received PEG 3350 monotherapy and group B received PEG 3350 and sodium picosulphate combination therapy.

The passage of watery stools was taken as the indicator of successful disimpaction. All the patients were followed up telephonically till the successful disimpaction was achieved or completed 7-day disimpaction therapy. The time to disimpaction from the day of initiation of therapy was noted for each patient. The patients who did not pass watery stools, even after completing 7-day treatment, were taken as failure of disimpaction therapy. The success rates and mean time to disimpaction in two treatment groups were computed and compared.

Statistical analysis

SPSS version 20.0 was used for data analysis. The qualitative variables were reported as percentage and quantitative variables as mean±SD. Fisher's Exact test was used for comparing categorical variables in two unrelated samples. The Kolmogorov-Smirnov test was used to assess the normality of the data. The difference between continuous variables in two unrelated samples was analysed using Mann Whitney U-test in non-normally distributed data and student-t test in normally distributed data. A p value of 0.05 or less was taken as statistically significant.

RESULTS

Children meeting our inclusion and exclusion criteria were enrolled in the study after obtaining informed consent from parents or LAR (legally acceptable representative) and assent from children as per predesigned data recording format. The selected patients were then randomized to group A, who received PEG 3350 monotherapy (1.5-2 gm/kg/day) and group B, who received combined PEG 3350 (1.5-2 gm/kg/day) plus sodium picosulfate (5 ml/day) therapy for disimpaction (Figure 1).

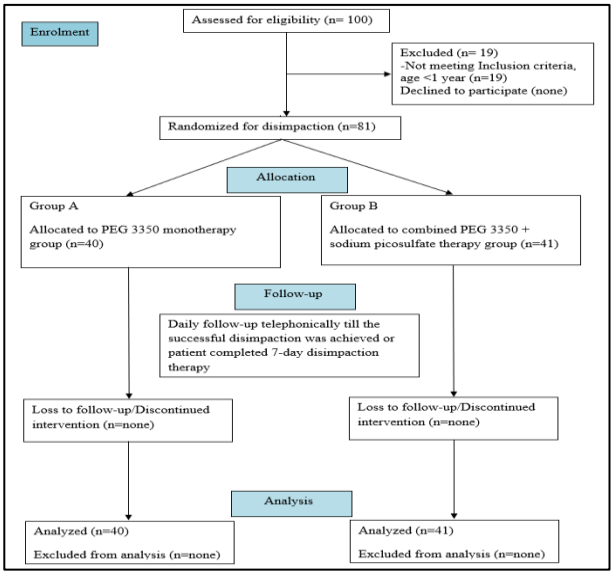

Figure 1: Flow chart of study design.

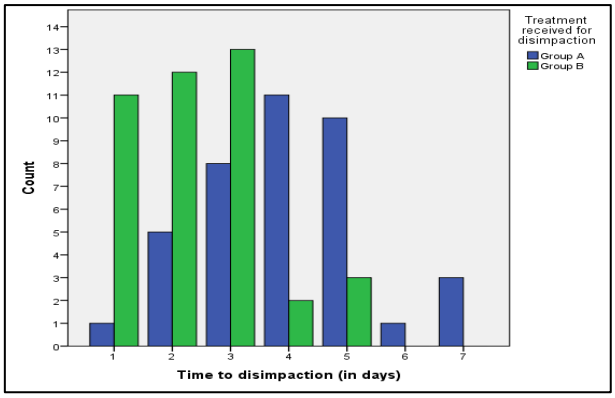

Figure 2: Time to disimpaction (in days) against the frequency observed in PEG 3350 monotherapy group (group A) vs combined PEG 3350 + sodium picosulfate therapy group (group B).

Socio-demographic profiles, anthropometric parameters and presenting symptoms of FC (i.e., defecation frequency of ≤2/week, presence of encopresis, history of painful/hard bowel movements, history of retentive posturing, presence of palpable fecaloma and the history of large diameter stools that can obstruct the toilet) had a similar distribution in both the groups (Table 1). There was no loss to follow-up of patients and/or voluntary withdrawal of patient from the study. The mean±SD time to disimpaction in group A was 4.00±1.43 days, with a range of 1 to 7 days. While in group B, it was 2.37±1.16 days, with a range of 1 to 5 days (Figure 2). The mean time to disimpaction was found to be significantly lower ($p<0.001$) for group B compared to group A (Table 2).

Table 1: Baseline characteristics in PEG 3350 monotherapy (group A) and combined PEG3350 + sodium picosulfate therapy (group B) groups.

		Group A (n=40)	Group B (n=41)	P value
Age, in years (mean±SD)		5.77±3.87	5.93±4.15	0.94
Gender	Females	55.0% (n=22)	53.7% (n=22)	1.00
	Males	45.0% (n=18)	46.3% (n=19)	
Community	Urban	27.5% (n=11)	21.95% (n=9)	0.61
	Rural	72.5% (n=29)	78.05% (n=32)	
Socioeconomic class	Upper	2.5% (n=1)	2.44% (n=1)	0.87
	Upper middle	55.0% (n=22)	43.9% (n=18)	
	Lower middle	35.0% (n=14)	41.46% (n=17)	
	Upper lower	5.0% (n=2)	9.76% (n=4)	
	Lower	2.5% (n=1)	2.44% (n=1)	
Weight, in kg (nean±SD)		17.97±9.14	19.67±12.63	0.69
Height, in cm (mean±SD)		109.25±26.32	107.55±24.79	0.76
Defecation frequency of ≤2/week		52.5% (n=21)	58.5% (n=24)	0.66
Presence of encopresis		15.0% (n=6)	19.5% (n=8)	0.77
History of painful/hard bowel movements		90.0% (n=36)	92.7% (n=38)	0.71
History of retentive posturing		75.0% (n=30)	65.85% (n=27)	0.47
Presence of palpable fecaloma		82.5% (n=33)	92.7% (n=38)	0.15
History of large diameter stools that can obstruct the toilet		17.5% (n=7)	14.63% (n=6)	0.77

Table 2: Comparison of time to disimpaction between patients achieving successful disimpaction in two groups.

Time to disimpaction (days)	Group A (n=39)	Group B (n=41)	P value
Mean	4.00	2.37	<0.001
SD	1.43	1.16	
Median	4.00	2.00	
Range	1-7	1-5	

Table 3: Comparison between percentage of patients achieving successful disimpaction in two groups.

Successful disimpaction	Group A (n=40)	Group B (n=41)	P value
Yes	97.5% (n=39)	100.0% (n=41)	0.49
No	2.5% (n=1)	0% (n=0)	

The successful disimpaction was achieved in all the group B patients (n=41). While among group A patients (n=40), successful disimpaction was achieved in 39 patients and 1 patient failed to respond to 7-day PEG 3350 monotherapy. The only patient who did not respond to 7-day PEG therapy was then administered combined PEG + sodium picosulfate therapy and the successful resolution of impaction was observed in 24 hours. Though differences observed were not statistically significant (p=0.49) at the end of 7 days (Table 3).

DISCUSSION

PEG acts as an osmotic laxative. It forms hydrogen bonds with water molecules, in a ratio of 100 water molecules for 1 PEG molecule leading to an increase in colonic water content. After oral intake, stool consistency improves within 24-48 hours.[11]

Sodium picosulfate acts as stimulant laxative and causes mild inflammation in intestines which leads to accumulation of water and electrolytes and stimulation of intestinal motility.[12]

Youssef et al did a prospective, parallel group study to assess the efficacy of PEG 3350 in the treatment of pediatric fecal impaction. 40 subjects, 3-18 years of age, were randomized to receive PEG 3350 in a dose of 0.25 gm/kg/d, 0.5 gm/kg/d, 1.0 g/kg/d, or 1.5 g/kg/d for 3 days. This study showed that 95% of children who received 1.0-1.5 gm/kg/d PEG 3350 were disimpacted, while only 55% of those who received 0.25-0.5 gm/kg/d were disimpacted.[13]

Jordan-Ely et al did a retrospective study to determine the efficacy of combination therapy of PEG (given on day 1 and 2) and sodium picosulfate (given on day 2 and 3) for treating fecal impaction. It was observed that all children (n=44) were successfully disimpacted.[14]

The study conducted by Acharyya et al demonstrated the superior efficacy of combined PEG plus sodium picosulfate therapy over PEG 3350 monotherapy.[8] However, disimpaction treatment in their study was done on hospitalized patients for two days only, followed by maintenance treatment for at least 10 months. Their findings of early disimpaction phase correlate with our result. In our study, the mean time to disimpaction was found to be significantly lower (p<0.001) for combined PEG + sodium picosulfate therapy (2.37±1.16 days) compared to the PEG 3350 monotherapy (4.00±1.43 days). No statistically significant differences (p=0.49) were observed in successful resolution of impaction in pediatric FC patients in either of the 2 groups: combined PEG + sodium picosulfate therapy group (success rate=100%) versus the PEG 3350 monotherapy group (success rate=97.5%). No adverse events were reported in either group.

Thus, the combination therapy of PEG 3350 and sodium picosulfate can be used for achieving early disimpaction in pediatric FC patients on outpatient basis. Major limitation of our study is that it was an open label study.

CONCLUSION

Combined PEG 3350 and sodium picosulfate therapy significantly reduces the disimpaction time when compared with PEG 3350 monotherapy in pediatric population, however both the therapies appear similar in achieving successful disimpaction.

ACKNOWLEDGEMENTS

We wish to acknowledge the assistance of Dr. Kamlesh Sharma, Assistant Professor, Community Medicine, Dr. Y. S. Parmar Medical College, Nahan District, Sirmaur, Himachal Pradesh, India in calculation of sample size for given study. Also, we would like to acknowledge the valuable assistance of entire department of pharmacology, nursing staff of pediatrics ward and all the patients who participated in the present study with full patience in contributing to the successful conduct of the study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Shinghal U, Sharma S, Kaundal PK. Comparative efficacy of polyethylene glycol 3350 monotherapy against polyethylene glycol 3350 plus sodium picosulfate combined therapy in treating fecal impaction in pediatric functional constipation patients. Int J Basic Clin Pharmacol 2023;12:551-5.