Pediatr Gastroenterol Hepatol Nutr. 2021 Mar;24(2):230-237
https://doi.org/10.5223/pghn.2021.24.2.230
pISSN 2234-8646·eISSN 2234-8840

Pediatric Gastroenterology, Hepatology & Nutrition
pghn

Short Communication

Polyethylene Glycol Plus Electrolytes with Stimulant Laxative in Paediatric Faecal Disimpaction: A Randomised Controlled Study

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Received: May 26, 2020
1st Revised: Jul 26, 2020
2nd Revised: Sep 7, 2020
Accepted: Oct 2, 2020

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Conflict of Interest
The authors have no financial conflicts of interest.

ABSTRACT

Functional constipation is common in the paediatric population all over the world. Effective disimpaction to evacuate the impacted faecal matter forms an essential initial step in the management of constipation. Though different regimens of polyethylene glycol 3350 with electrolytes (PEG+E) are accepted as the prime medication for disimpaction, response is not always satisfactory. A randomised prospective study was undertaken, in a tertiary paediatric Gastroenterology centre to find out the outcome of a 2-day disimpaction when a stimulant laxative sodium picosulphate was added to PEG3350+E (PEG+E+PS group) and comparing it with the outcome using PEG3350+E (PEG+E group) alone. Hundred and one children were randomised into two groups to receive PEG+E+PS and PEG+E. Results revealed that PEG+E+PS group proved significantly superior to PEG+E group in most of the efficacy-parameters in terms of disimpaction as well as long-term management of constipation. Though stimulant laxatives are being used for disimpaction, comparative data are lacking. This was the 1st such comparative study looking at the efficacy of these two processes of disimpaction along with long term effect on treatment.

Keywords: Paediatric; Functional; Constipation; Polyethylene glycol+electrolytes; Faecal Incontinence; Laxative; Sodium picosulphate

INTRODUCTION

Chronic constipation is not uncommon in Asian countries [1,2]. Disimpaction is a very important initial step to dislodge the hard, impacted faeces to achieve the eventual success of any management protocol for constipation. Oral polyethylene glycol 3350 with electrolytes (PEG+E) is accepted as the best available medication to undertake this process of disimpaction effectively [3,4]. Standard recommended dose of PEG followed in most centers are either a lavage solution (25 mL/kg/hr) administered over 4 hours or 1.5 mg/kg/day oral dose given for 3–6 days at home.

National Institute of Clinical Excellence (NICE) and European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) recommend the addition of

Table 1. Showing dosage regimen in both the groups

2–5 yr	9 am -- Syr domperidone (5 mL/5 mg) 5 mL*,†
10–20 kg	9.30 am PEG+E (Movicol Paed) sachet 7 sachet (45 gm of PEG3350) in 450 mL of water/noncarbonated beverage to be finished over 2 hr*,†
	Syr PS (5 mL/5 mg) 5 mL at 9 am 5 mL at 2 pm†
>5–10 yr	9 am -- Syr domperidone (5 mL/5 mg) 7.5 mL*,†
>20–30 kg	9.30 am PEG+E (Movicol Paed) sachet 11 sachets (72 gm of PEG3350) in 700 mL of water/noncarbonated beverage to be finished over 2 hr*,†
	Syr PS (5 mL/5 mg) 7.5 mL at 9 am 7.5 mL at 2 pm†
>10–15 yr	9 am -- Syr domperidone (5 mL/5 mg) 10 mL*,†
>30–40 kg	9.30 am PEG+E (Movicol Paed) sachet 14 sachets (91 gm of PEG3350 in 900 mL of water/noncarbonated beverage to be finished over 2 hr*,†
	Syr sodium PS (5 mL/5 mg) 10 mL at 9 am 10 mL at 2 pm†
Take weight for dosage if it is higher.	
Breakfast should be given between 8 to 8.30 am.	
No food allowed while taking PEG+E. Lunch is given after 1.30 pm	

PEG: polyethylene glycol, E: electrolytes, PS: sodium picosulphate.
*PEG+E, †PEG+E+PS.

a stimulant laxative if oral PEG+E fails to disimpact [3]. But recommendation is lacking regarding PEG+E with stimulant for disimpaction purpose. Our centre was using an age based dosage regime of PEG+E for 2–3 days for disimpaction (**Table 1**) with results not as satisfactory as expected. After addition of a stimulant laxative with the age wise PEG+E dosage followed in our center attained a faster and better result evacuating the fecal load. So the following study was planned with a primary goal to compare the efficacy of both the regimen (PEG3350+E alone and PEG3350+E with stimulant laxative) for disimpaction and a secondary goal to find out any noteworthy effect of these two regimens on the long term therapy of constipation.

MATERIALS AND METHODS

This prospective randomized controlled study had been carried out in a tertiary Paediatric GE center in Kolkata, India from May 2015 to December 2017. As there was a long follow up, recruitment and intervention for disimpaction was carried out in the 1st 8 months of the study period (i.e., from May 2015 to December 2015).

Study design

This is a single blind randomized study where children undergoing disimpaction for constipation treatment were randomized to either PEG3350+E only or PEG3350+E with a stimulant laxative.

Participants

Children aged 2–14 years, suffering from functional constipation (diagnosed by ROME III criteria) were included. All children were investigated to rule out Hypothyroidism, Coeliac Disease, hypercalcaemia, chronic kidney disease & diabetes and if found positive were excluded from the study. Faecal impaction was decided on abdominal examination where a faecal mass was palpable or in abdominal X-ray (done in children who came with severe abdominal pain). Digital rectal examination was avoided to prevent the augmentation of fear associated with defecation. All children with faecal incontinence irrespective of faecal mass were included.

Inclusion criteria

1) All children of functional constipation with faecal mass.
2) All children of functional constipation with faecal incontinence irrespective of faecal mass.

https://doi.org/10.5223/pghn.2021.24.2.230

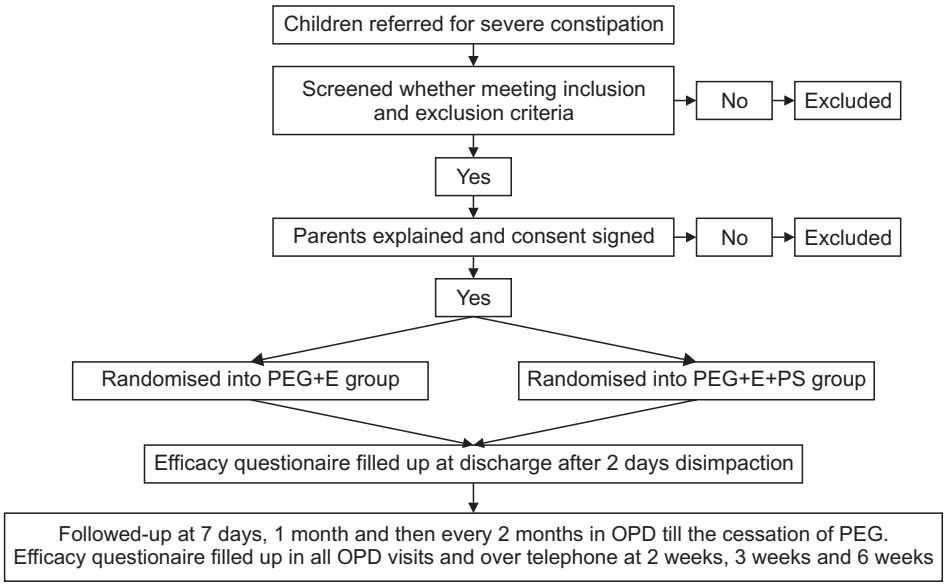

Fig. 1. Flow chart of study design.
PEG: polyethylene glycol, E: electrolytes, PS: sodium picosulphate, OPD: Out-Patients Department.

Exclusion criteria

Children with coeliac disease, diabetes, hypothyroidism, hypercalcaemia, chronic renal disease or other chronic ailments and neuro-disability.

Intervention

Children meeting our inclusion and exclusion criteria were recruited after formal consenting (**Fig. 1**). They were randomized to receive PEG3350+E solution alone (PEG+E group) or PEG3350+E with sodium picosulphate (PEG+E+PS group) for disimpaction as per the dosage mentioned in **Table 1** consecutively for 2 days. All the children were hospitalized for 2 days to receive the treatment and to be observed closely. Children were given sitz-bath 4 times/day to reduce any pain associated with defecation and ease up the act.

A written questionnaire containing parameters namely number of stools on 1st and 2nd day, nausea, vomiting, abdominal distension & pain during intake of medication, stool frequencies achieved during 1st and 2nd week after the treatment, reduction of perianal pain/discomfort, time of cessation of incontinence, need for rectal enema and global satisfaction of parents was filled up independently by a departmental coordinator, designated for the study; before discharge, during the outpatient visit at 1 week, 1 month, then every 2 months and over the telephone at 2 weeks, 3 weeks, and 6 weeks. Maintenance treatment was followed from day 3 with oral PEG3350+E along with parental education and behavioral modifications in all of them. At discharge maintenance was started with half of the disimpaction dose for the initial 5 days then continued at 0.8–1 g/kg/day according to the behavior of the child. All children were followed up in outpatients at 1 week, 1 month and then every 2 months until the cessation of medication. Medications were continued for 10–18 months and then tapered according to the developed habit and tolerance of the patient. All children were advised to continue treatment at least for 10 months and assessment for tapering was considered only after 10 months. Criteria for tapering the dose was regular bowel habit (once/day at least 6 days/week as well as complete absence of incontinence and anal pain for the prior 3 months during assessment at 10 month-visit. Dose of PEG3350+E

https://doi.org/10.5223/pghn.2021.24.2.230

was tapered by half a sachet (i.e., 3.25 gm PEG3350) every 4 weeks until it dropped to a dose of 3.25 gm PEG3350 which was continued for 1 month and then treatment was stopped. Parents were instructed to go back to the previous month's dose if children faced problem with any tapered dose and to retry again after 1 month. The span of treatment was noted in each patient who completed follow-up still cessation of treatment.

Ethical approval

Ethical Committee approval was obtained from the AMRI Hospitals Institutional Ethics Committee (Approval No. AMRI-EC/AP-25/2015-16).

Sample size calculation

Keeping a standard power of 80% and alpha of 0.05, a sample size of each arm was calculated as 60.

Method for randomization

For randomization permuted block randomization method was used. It was done in a ratio of 2:2. This was done in a block of 4, 2 in the PEG+E group and 2 in the PEG+E+PS group. There were 6 possible combinations all were given specific numbers. We then used a random number generator to make a list of random numbers from 1 to 6 and used this list to randomize. This list was kept with an investigator (CB) who was not involved with the recruitment or initial data collection. Group allocation was done after calling this investigator. As it was a single blind study the investigator was blind to the intervention not the participant.

Statistical calculation

Statistical calculation was done using simple mean and standard deviation calculator and ANOVA for one way calculation of a variance. Fisher's Exact test was applied for comparison of categorical variables. A *p*-value of 0.05 or less was accepted as significant.

RESULTS

During the first 8 months of recruitment period 120 children were referred to us with severe constipation. Twelve children refused to take part in the study and the other 9 were excluded for secondary aetiologies. Rest 101 consecutive children participated in the study though the calculated sample size required more. Fifty received PEG+E and 51 received PEG+E with PS.

Fifteen (14.8%) of them needed an abdominal X-ray as they came with abdominal pain Demographic profiles were comparable in both the groups (**Table 2**). Girls were more (61) than boys (40). The mean duration of constipation was 9.5±2.8 months and 9.6±3 months in each group. A 2/3rd children in both groups received Lactulose for treatment before referral

Table 2. Demography and base line characteristics of the two groups

Demography & efficacy parameters	PEG+E (n=50)	PEG+E+PS (n=51)	*p*-value
Age (mo)	69.9 (24.9)	70 (25.2)	0.99
Sex (female:male)	31:19	30:21	
Duration of constipation (mo)	9.5 (2.8)	9.6 (3)	0.98
No of patients with incontinence	23 (46.0)	21 (41.2)	0.69
Medicine received before referral (lactulose:other combinations)	31:19	34:17	0.68

Values are presented as mean (standard deviation), number only, or number (%).
PEG: polyethylene glycol, E: electrolytes, PS: sodium picosulphate.

https://doi.org/10.5223/pghn.2021.24.2.230

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Table 3. Efficacy parameters of the two groups

Efficacy parameters	PEG+E (n=50)	PEG+E+PS (n=51)	*p*-value
Primary outcomes			
No of stools achieved on the 1st day	2.5 (0.92)	5 (1.02)	<0.0001
No of stools achieved on the 2nd day	5 (1.02)	7 (1.12)	0.0001
Reduction of perianal pain during defecation (2nd day)	40 (80.0)	46 (90.2)	0.1722
Need for Enema to initiate evacuation	5 (10.0)	1 (2.0)	0.112
Global satisfaction of parents* (during disimpaction)	3.12 (0.52)	3.15 (0.5)	0.93
Side effects			
Abdominal distension and pain (no of children)	15 (1.2)	3 (1.03)	<0.0001
Nausea/vomiting during taking medication	2	3	1
Secondary outcome			
Cessation of incontinence (mean day)	30 (2.5)	16 (1.6)	<0.00001
Mean stool frequency achieved on 1st wk	3.5 (0.84)	7.2 (1.2)	<0.001
Mean stool frequency achieved on 2nd wk	7.4 (1.5)	14.4 (2.1)	<0.0001
No of children reimpacted (6 mo)	4 (8.0)	0 (0.0)	0.039
Total duration of treatment (with tapering and cessation of maintainance)	19.9 (3.7)	17 (2.0)	0.0005

Values are presented as mean (standard deviation), number (%), or number only.
PEG: polyethylene glycol, E: electrolytes, PS: sodium picosulphate.
*5: very happy, 4: happy, 3: satisfactory, 2: less satisfactory, 1: no satisfaction.

and rest received various other medicines including PEG, Homeopathic and Ayurvedic preparations. Fecal incontinence was recorded in 46% and 41% of children in each group.

Outcome

All children could take the PEG+E solution orally well, without the need for NG insertion, though 20 children (20%) took about 3 hours to finish it. Response parameters were recorded from parents on the questionnaire form were calculated for significance (**Table 3**). In terms of frequency of stool in the 1st and 2nd day and development of abdominal distension or pain, PEG+E+PS group did significantly better. Children in the PEG+E+PS group achieved more stool frequency in the 1st and 2nd week with the earlier cessation of incontinence compared to the PEG+E group. By 6 weeks it was found that both groups reached a mean stool frequency of 6–8/week.

Initial 6 months' follow-up was completed by all (100%) children of each group. There-after total of 23 patients (9 in the PEG+E group & 14 in the PEG+E+PS group) were lost to follow-up. The number of children re-impacted during 1st 6 months of treatment was 4 and none respectively in the PEG+E and PEG+E+PS groups which were marginally significant. The mean duration of treatment in PEG+E+PS group was 17 months which was also significantly less compared to the PEG+E group (20 months) (**Table 3**).

DISCUSSION

Disimpaction forms an integral fundamental step in the management of constipation in children [2]. But there is dearth of data regarding the efficacy of disimpaction treatment-regimes followed in different Paediatric centers of the world. In India there is no such data available till now. Most of the Indian Paediatric GE centers administer a PEG solution 20–25 mL/kg/hour over 4 hours for disimpaction which is again repeated in next two days if required [1]. We had found our patients to be less compliant to that dosage and a large fraction of children were requiring NG tube for administration of the medicine. So our centre had been following a regimen containing PEG+E (**Table 1**) with better patient-compliance but

https://doi.org/10.5223/pghn.2021.24.2.230

with variable efficacy. This study showed that adding a stimulant laxative with PEG3350+E definitely made the treatment more efficacious along with good patient acceptability. This finding corresponds with a recent retrospective study in Australia by Jordan-Ely et al. [5] using PEG+E with PS (from 2nd day) depicting the regimen to be effective in controlling severe disimpaction. They conducted their study as outpatient treatment for 4 days and did not compare it with any other regimen [5].

High-dose PEG given orally is associated with a higher frequency of fecal incontinence during treatment of the fecal impaction compared with enema use; however, based on the argument that PEG can be administered orally, ESPGHAN AND NASPGHAN working group decided to prefer PEG [4]. Guest et al. [6] in a retrospective review of 112 children found that PEG3350 is a clinically effective and cost-effective treatment for the disimpaction of children suffering from faecal impaction compared to enemas and suppositories or a manual evacuation. NICE as well as ESPGHAN guidelines states that use of rectal suppositories should be contemplated when oral regimen does not work [3]. In this study usage of enema was restricted to a very small number of children (only 5 cases in total) to initiate bowel movement if they failed to respond at the end of the 1st day. In contrast to Candy et al. [7] who described a zero reimpaction rate within 12 weeks after disimpaction with PEG+E and with PEG+E maintenance treatment, this study found re-impaction in 4 patients (within 1st 6 months) in the PEG+E group (4 vs. 0) which was marginally significant. Post disimpaction long term comparison between these two groups showed that PEG+E+PS group completed treatment relatively earlier (**Table 3**). Therefore this study again proved that an effective disimpaction regime was beneficial for the long term treatment goal of constipation as suggested earlier [4,7].

PEG3350 with electrolytes was found to be more effective compared to mineral oil [8] and magnesium citrate [9]. Yussef et al. [10] concluded that a dose of 1.5 mg/kg to be the most effective for disimpaction after trying different lower doses. Our regimen used slightly higher dose of 2–4 gm/kg/day of PEG3350 which was accepted and tolerated well by the children with negligible side effects. The reason behind this higher dose was that previous use of 1.5 g/kg was not found satisfactory for our children with long standing severe constipation and we wanted a short and effective disimpaction regime producing an effect like colon cleansing. This is still lower than the recommended maximum colon cleansing daily dose (5.9 gm/kg) advocated through the PEG+E lavage-solution (klean-prep) over 4 hours [11]. Most of the Indian centres also follow this lavage protocol at this dose over 4 hours for in-patients [1]. The dosage in our regimen was also much lower than Ingebo and Heyman [12] who administered even higher than the BNF recommended dose in a day (33 gm/kg) spread over several hours via nasogastric tube for the treatment of faecal incontinence. The advantage of the current regimen was that it could be administered orally in all without any need of nasogastric tube. Though hospital admission was mandatory in this study for the close observation purpose, after this trial, this regimen was being effectively used at home for 2 days followed by reassessment of children after 2 days to evaluate the response and to decide about the maintenance dosage. This emerged as a very well accepted regime by all the parents.

Limitations of this study were a hospital admission of all children for close observations, single-blinded, an amount of recall bias (as data collected on weekly basis after the hospital admission) and results were based on clinical response without any objective evidence (like Xray) at the start and end of the study unlike the study protocol of Jordan-Ely et al. [5].

https://doi.org/10.5223/pghn.2021.24.2.230

In conclusion, to the best of our knowledge this was the first prospective comparative analysis, demonstrating the advantage of PEG+E+PS over sole PEG+E in the treatment of childhood fecal disimpaction. It also showed that a slight increased dose of PEG3350+E for disimpaction is safe and well accepted orally. This study proved once again that a successful disimpaction is very beneficial for the long term management of severe constipation. In short disimpction regimen used had been proved to be brief, safe and very effective for immediate and long term goals. Larger multicentre studies are needed to further validate our findings.

ACKNOWLEDGEMENTS

We would like to acknowledge the contribution of Ms Swagata De for collecting information from parents in the Questionaire and Ms Astha Acharyya for manuscript English language correction. We would like to thank my teachers Dr Mike Thomson and Dr HR Jenkins as the study design was influenced by their paper 'Polyethylene glycol 3350 plus electrolytes for chronic constipation in children: a double blind, placebo controlled, crossover study' in Arch Dis Child 2007;92:996-1000.

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