Constipation management in Children:

Dr.Binod Kumar Singh

Professor & Head
Dept. of Pediatrics, NMCH, Patna
IAP State President, Bihar- 2019
CIAP Executive board member-2015
NNF State president, Bihar- 2014
IAP State secretary,Bihar-2010-2011
NNF State secretary,Bihar-2008-2009
Fellow of Indian Academy of Pediatrics (FIAP)

- Consultant Neonatologist & Pediatrician

Shiv Shishu Hospital :K-208, P.C Colony,Hanuman Nagar,
Patna – 800020
Web site : www.shivshishuhospital.com

Introduction

- Constipation is an underestimated but common health problem worldwide, decreasing the quality of life
- Functional constipation (FC) is a common childhood problem with varied prevalence between geographic regions
- In Asia (including infants–adolescents), the prevalence is estimated between 0.5% and 29.6%. Prevalence data on constipation in Indian children is sparse
- A study from Andhra Pradesh reported that the prevalence of functional constipation was noted in 30.8% with female preponderance and incidence was more in the age group of 2-4 years
- A North Indian study showed that FC is the most common cause of constipation in children in North India, and only 13% patients have an organic pathology
- FC is commonly seen among toddlers and preschool children, and in 17% to 40% of cases, constipation starts in first year of life

Normal Frequency of Bowel movements in Infants and Children

AAFP

ispghan
INDIAN SOCIETY OF PEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION

Normal Frequency of Bowel Movements in Infants and children		
Age	Mean number of bowel movements per week	Mean number of bowel movements per week
0 to 3 months: breastfed	5 to 40	2.9
0 to 3 months: formula-fed	5 to 28	2.0
6 to 12 months	5 to 28	1.8
1 to 3 years	4 to 21	1.4
>3 years	3 to 14	1.0

Normal Stool frequency in Indian Children	
Age	Frequency
<1 month	3-4 times/day
1 month to 1 year	1.5-2 times/day
1 to 2 year	1-2 times/day
Older than 2 year age	1 time/day

Definition of Constipation: Indian Children

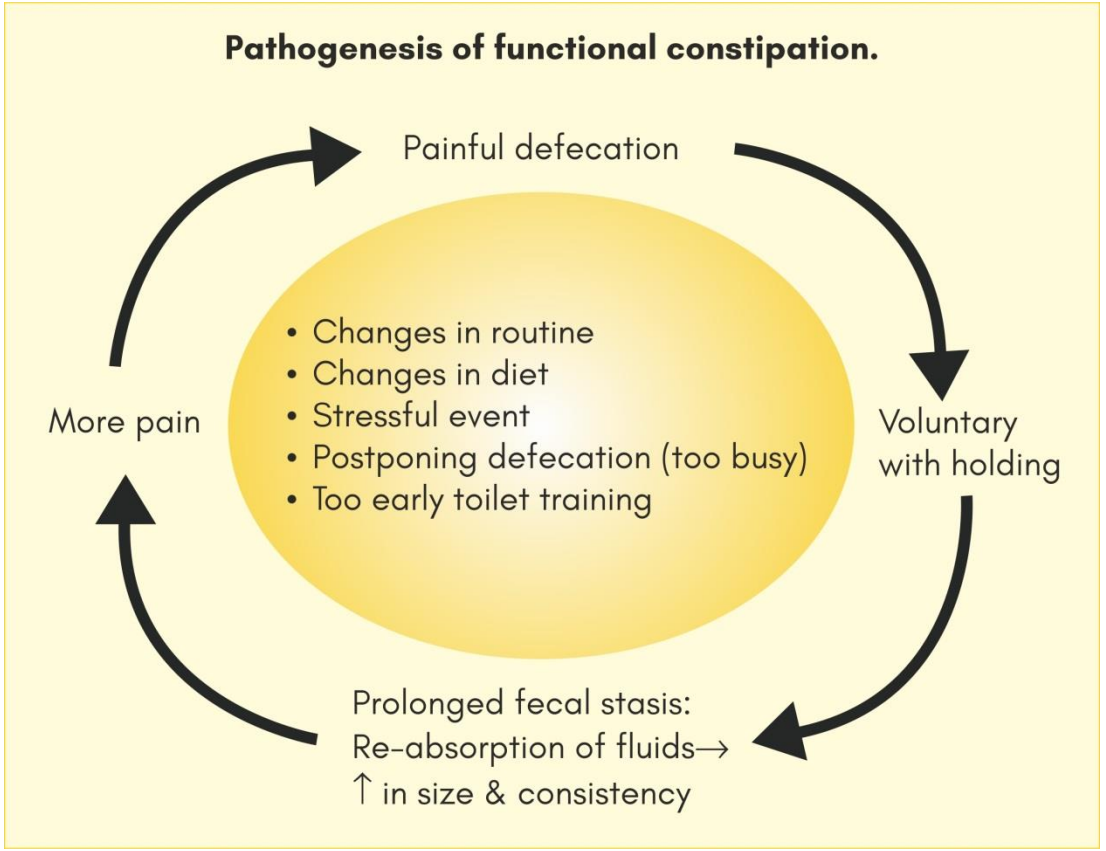
- Constipation: A delay or difficulty in defecation sufficient to cause significant distress to the patient is defined as constipation
- Based on the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) guidelines, Rome III criteria and expert opinion, the definition recommended for application in Indian children is given in Box 1

Box 1. Definition of Constipation for use in Indian Children

- Duration of more than 4 weeks for all ages; and
- Presence of ≥2 of the following: (a) defecation frequency ≤2 times per week, (b) fecal incontinence ≥1 times per week after the acquisition of toileting skills, (c) history of excessive stool retention, (d) history of painful or hard bowel movements, (e) presence of a large mass in the rectum or on per abdomen examination, (f) history of large-diameter stools that may obstruct the toilet (This may not be elicitable for majority of Indian children who do not use the Western type of toilet)

Pathogenesis

- Painful bowel movement leads to voluntary withholding of stools by the child
- Different events give rise to large, hard stool
- Hard stools lead to pain and Child fearfully determines to avoid defecation by all of means
- Withholding of feces leads to harder stools
- Successive retention of stools in rectum make them larger
- Severe “stool withholding maneuvers” are seen
- Thus a vicious cycle sets in (Fig 1)



NONORGANIC (FUNCTIONAL- 85%)

ORGANIC

Anatomic

- Anal stenosis , atresia with fistula, imperforate anus .
- Anteriorly displaced anus
- intestinal stricture
- Anal stricture

Abnormal musculature

- Prune –belly syndrome
- Gastroschisis
- Down syndrome
- Muscular dystrophy

Intestinal nerve or muscle abnormality

- Hirschsprung disease
- Pseudoobstruction
- Intestinal neuronal dysplasia
- Spinal cord lesion
- Tethered cord
- Autonomic neuropathy
- Spinal cord trauma
- Spina bifida
- Chagas disease

Drugs

- Anticholinergics
- narcotics
- Methyphenidate
- Phenytoin
- Vitamin D intoxication
- Calcium channel blocking agent

Metabolic disorder

- Hypokalemia
- Hypercalcemia
- Hypothyroidism
- Diabetes mellitus, diabetes insipidus
- Porphyria

Intestinal Disorder

- Celiac disease
- Cow’s milk protein intolerance
- Cystic fibrosis
- Inflammatory bowel disease
- Tumor
- SLE
- Scleroderma

Psychiatric Diagnosis

- Anorexia nervosa

What does ISPGHAN and IAP Guidelines say?

Indian Society of Pediatric Gastroenterology, Hepatology and Nutrition and Pediatric Gastroenterology Chapter of Indian Academy of Pediatrics

History and Evaluation

- History and examination are relevant to evaluate different factors
  - **Dietary history:** Details of diet should be taken: intake of fruits and vegetables and refined foods (e.g., bakery products), beverages etc. in older children, nature of feeds (breast vs. top feeds) and
  - Details of supplementary feeds in younger babies
  - **Evaluation:** Patients should be examined thoroughly with proper growth assessment to rule out an organic etiology
  - Lower abdomen should be palpated for fecoliths (soft or hard indentable masses)

History and Evaluation (contd..)

- Digital rectal examination (DRE) (index finger in an older child or little finger in an infant) helps in the following:

  a. Presence of fecal impaction (seen in 50-70% children with functional constipation and is diagnosed in the presence of a hard mass (fecal mass) in the lower abdomen or presence of large, hard stools (fecolith) on Digital rectal examination (DRE)

  b. Diagnosis of Hirschprung's disease (empty rectum, gush of stools/air on withdrawal of finger), and

  c. Sacral mass lesion (palpable mass)

- However, Digital rectal examination (DRE) is not essential in all cases or at all visits

Investigations and Red flags

Red flags suggestive of organic constipation:

- Delayed passage of meconium
- Onset in infancy
- Ribbon or pellet stools
- Bilious vomiting
- Uniform abdominal distension
- Failure to thrive
- Recurrent lower respiratory infections
- Cold intolerance
- Neuro-developmental delay or regression
- Gush of stools on DRE
- Anal malformations
- Abnormal neurological examination (paraspinal, lower limbs and anorectal reflexes)

95% children with constipation have functional constipation and do not need any investigations

Children with red flags suggestive of organic etiology or those who are diagnosed as functional constipation but fail to respond to therapy need diagnostic evaluation

A plain erect X-ray abdomen or barium enema is not required as a routine investigation in all cases

Investigations

1 Ractal biopsy - HD,Neuronal intestinal dysplasia,
hypoganglionosis

2 Anorectal manometry

3 MRI Lumbosacral spine

4 colonic transitory study

a . Radio opaque marker.....

b. scintigraphy

5 Metabolic , endocrive & others

- Hypothyroidism
- cystic fibrosis
- hypercalcemia
- Coeliac disease
- lead poisoning

Management

1) Patient counselling:

- Pathophysiological aspects inclusive of objective of treatment should be explained to the parents
- Cause of functional constipation, preferably with a diagram
- Any precipitating factors identified should be eliminated (e.g. in a child with exclusive milk feeding, (semi) solid diet supplementation should be instituted; drugs causing constipation should be stopped; any psychosocial factor operating needs to be addressed)

2) Toilet Training: Should not be started before 24 months of age

- Follow the 'Rule of' 1: Toilet training to be done by one person, one routine (5 min after each major meal), one place, one word e.g. pooh/potty etc.

In a child with constipation:

- Make the child sit in the toilet, 2-3 times a day for 5-10 minutes after meals (within 30 minutes of meal intake)
- Make the defecation painless by treating anal fissures, if present
- Sit in squatting position in the Indian toilet or with foot rest in English toilet/potty seat
- Reward system (positive reinforcement) helps in motivating the child and avoiding child-parent conflict

Management

3) Diet, Fibre and Water intake:

- No well-conducted RCTs
- Daily fiber requirement is 0.5 gm/kg/day
- Initially adequate intake of fiber-rich diet (cereals, whole pulses with bran, vegetables etc.) is recommended
- High fiber diet chart should be given to parents (as per local practice)
- Restrict milk and encourage intake of semi-solids and solids in younger children and also ensure adequate intake of water

4) Medical therapy

- It consists of initial phase of disimpaction in patients with fecal impaction and a maintenance phase with laxatives

a. Disimpaction:

- Completely clear the colon so that no residual hard fecal matter is retained. Thereafter the maintenance laxative therapy can keep the bowel moving and empty so that there is no retention

There are two ways of disimpaction

  - One-time hospital based (100% success)
  - Home based in split doses (68-97% success)

- Rarely rectal enemas can be used as supplementary therapy
- Oral route is preferred as it non-invasive, has better patient acceptability, cleans the entire colon and is equally effective as rectal disimpaction
- Children undergoing disimpaction should be reviewed within one week of disimpaction to assess for re-impaction
- Maintenance therapy should be started only after effective disimpaction

Management

Table II Disimpaction			
Agent	**Dosage**	**Side effect**	**Comments**
Oral agents			
Polyethylene glycol* (at home)	1.5-2 g/kg/d in two divided doses for 3-6 d** only depending upon the clarity of rectal effluent	Loose stools, bloating/flatulence, nausea, vomiting	-
Polyethylene glycol solution for lavage (in hospital)	• 25 mL/kg/h oral or by nasogastric tube in young children • End point is clear rectal effluent • Young children may require intravenous fluids to maintain hydration	Nausea, vomiting, abdominal cramps, rarely electrolyte abnormality, pulmonary aspiration	Caution: During one-time disimpaction, watch for bloating, abdominal distension or fluid overload
Rectal agents			
Enemas (once per day)			
Saline	Neonate <1 kg; 5 mL; > 1 kg: 10 mL >1y: 6 mL/kg, once or twice/day		Not usually practised except in special situations
Phosphate soda (Proctoclysis enema 100 mL)	2-18y: 2.5 mL/kg, max 133 mL/dose	Hyperphosphatemia, Hypocalcemia	

Management

4) Medical therapy

b. Maintenance therapy:

Osmotic laxatives (OL): 2 main OL : Polyethylene glycol (PEG) and lactulose/ lactitol

- PEG is the first line of therapy and is more effective as compared to lactulose/lactitol.
- However in children <1 year of age, the only drug recommended is lactulose/ lactitol
- Second line of treatment is lactulose/lactitol which is safe for all ages
- Two osmotic agents like PEG and lactulose/lactitol should not be given simultaneously and combination therapy with two classes of laxatives is not recommended for children

Stimulant laxative:

- Used only as rescue therapy
- No RCTs on efficacy
- Given for shorter duration of 2-3 days

Behavioural therapy and biofeedback:

- Helpful when constipation is associated with behavioral co-morbidity or pelvic floor dysfunction.

Management

Table III Osmotic Laxatives for Maintenance Therapy			
Osmotic Laxative	**Dose**	**Side effects**	**Comments**
Polethylene Glycol	0.5-1 g/kg/day > 12 month age	Bloating, Abdominal pain/cramps, Vomiting, Loose stools	Safe for both short and long term use
Disaccharides			
Lactulose: non absorbable synthetic disaccharide, consists of 2 molecules of galactose and fructose	1 mo-12 mo: 2.5 mL BD; 1-5y: 2.5-10 mL BD; 5-18y: 5-20 mL BD	Abdominal distension Discomfort	Lactulose undergoes fermentation in the colon to yield short chain fatty acids, Co_2 and H_2
Lactitol (β-galactosido-sorbitol): monohydrate is a analogue of lactulose, consists of galactose and sorbitol	250 to 400 mg/kg/d (15 mL = 10 g of lactitol monohydrate		Lactitol is more palatable with better acceptability

Management

5) Follow up

- Record the stool history, associated symptoms, compliance with diet, medications and toilet-training
- Maintain Stool diary
- First follow-up is advised at 14 days to assess compliance
- Subsequently 1-2 monthly follow-up till normal bowel habit is attained. Further 3, monthly follow up for a minimum period of one year
- The maintenance dose may be increased or decreased to achieve daily passage of stools

Treatment Success

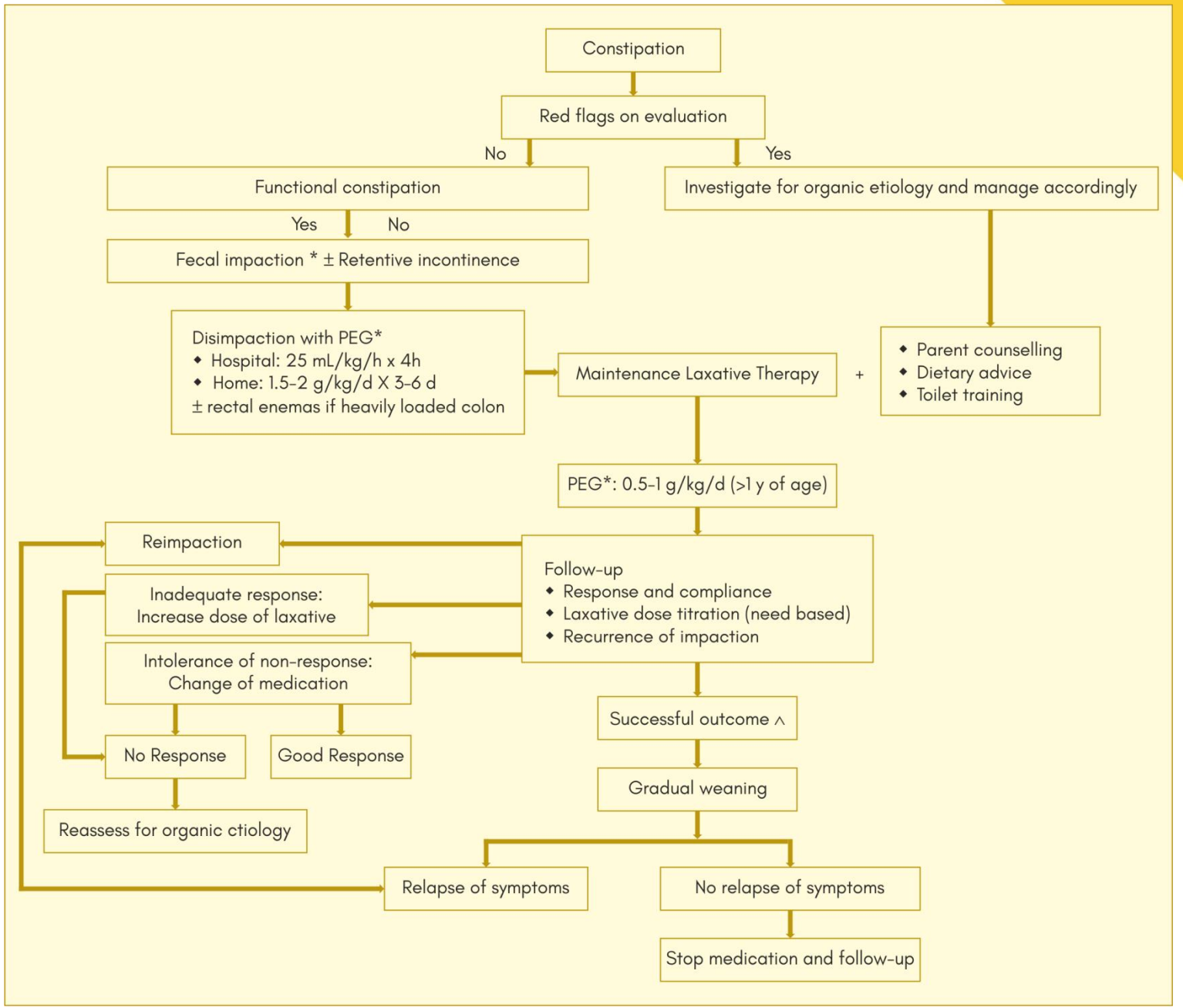
- Successful outcome of treatment should be defined as
  - Stool normalcy while on laxatives for a period of at least 4 weeks of initiation of therapy, and
  - Achievement of stool normalcy for a minimum period of 6 months before tapering
- Normalcy of stools should defined as daily, not hard, nor loose watery stools, with absence of pain, straining, bleeding, posturing or incontinence

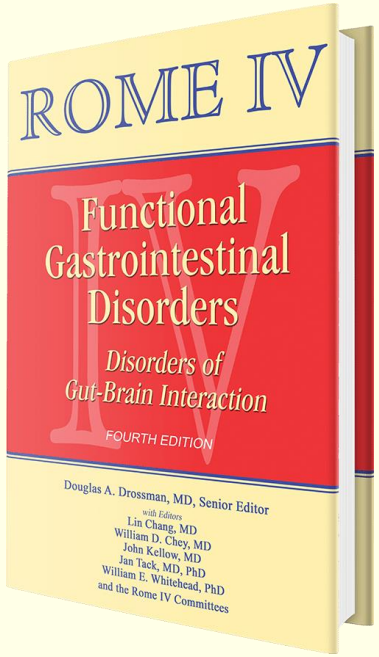
Indian Data

- Data from India show that 95% respond over a mean (SD) follow-up of 15.0 (16.7) months
- 18.4% patients have recurrence of symptoms on follow up; 10.5% of them require rescue disimpaction after a median duration of 5.5 (1.5-17) months of the first disimpaction

Algorithm: Management of Childhood Functional Constipation

- Functional constipation should be diagnosed in the absence of red flags. Impacted (incontinent) and non-impacted subgroups should be identified
- Management protocol should be adapted as per the algorithm shown.





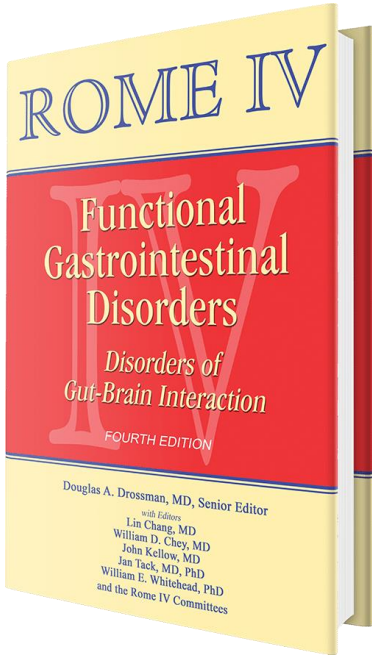
Functional Constipation: What does Rome IV say?

Diagnostic Criteria for Functional Constipation

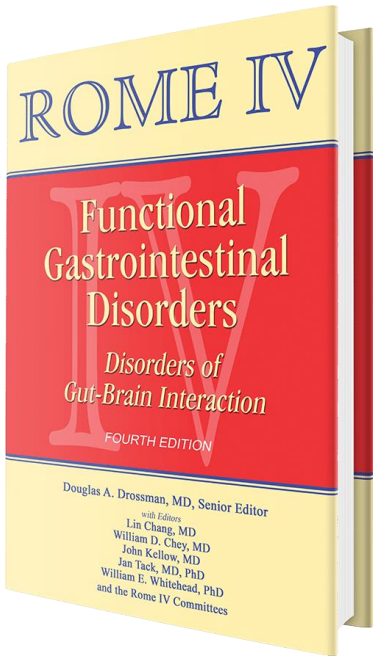
Must include 2 or more of the following occurring at least once per week for a minimum of 1 month with insufficient criteria for a diagnosis of irritable bowel syndrome:

1. 2 or fewer defecations in the toilet per week in a child of a developmental age of at least 4 years.
2. At least 1 episode of fecal incontinence per week
3. History of retentive posturing or excessive volitional stool retention
4. History of painful or hard bowel movements
5. Presence of a large fecal mass in the rectum
6. History of large diameter stools that can obstruct the toilet

After appropriate evaluation, the symptoms cannot be fully explained by another medical condition.



Clinical evaluation



Endorses the consensus guideline for the evaluation and treatment of the child with FC published by

ESPGHAN

NASPGHAN
North American Society for Pediatric Gastroenterology, Hepatology and Nutrition

Potential Alarm Features in Constipation

- Passage of meconium >48 in a term newborn
- Constipation starting in the first month of life
- Family history of Hirschsprung's disease
- Ribbon stools
- Blood in the stools in the absence of anal fissures
- Failure to thrive
- Bilious vomiting
- Severe abdominal distension
- Abnormal thyroid gland
- Abnormal position of the anus
- Absent anal or cremasteric reflex
- Decreased lower extremity strength/tone
- Sacral dimple
- Tuft of hair on spine
- Gluteal cleft deviation
- Anal scars

Clinical evaluation

Some of the recommendations from the guidelines are listed here:

1. ROME criteria are recommended for the definition of FC for all age groups
2. The diagnosis of FC is based on history and physical examination
3. Alarm signs and symptoms and diagnostic clues should be used to identify an underlying disease responsible for the constipation (Table)
4. If only one Rome criterion is present and the diagnosis of FC is uncertain, a digital examination of the anorectum is recommended to confirm the diagnosis and exclude underlying medical conditions.
5. There is no role for the routine use of an abdominal x-ray to diagnose FC

Clinical evaluation

6. A plain abdominal radiograph may be used in a child if fecal impaction is suspected but in whom physical examination is unreliable/not possible

7. Routine allergy testing for cow's milk allergy is not recommended in children with constipation in the absence of alarm symptoms

8. Laboratory testing to screen for hypothyroidism, celiac disease, and hypercalcemia is not recommended in children with constipation in the absence of alarm symptoms

9. The main indication to perform anorectal manometry in the evaluation of intractable constipation is to assess the presence of the rectoanal inhibitory reflex

10. Rectal biopsy is the gold standard for diagnosing Hirschsprung's disease

11. A barium enema should not be used as an initial diagnostic tool for the evaluation of FC

Treatment

- Education is as important as medical therapy. This should include:
  - Counseling families to recognize withholding behaviors and to use behavioral interventions, such as regular toileting, use of diaries to track stooling, and reward systems for successful evacuations
  - A normal fiber and fluid intake is recommended
- The pharmacologic approach comprises 2 steps: rectal or oral disimpaction for children who present with fecal impaction and maintenance therapy to prevent reaccumulation of feces using a variety of agents
- **Polyethylene glycol is first-line therapy for constipated children**

What does ESPGHAN and NASPGHAN Guidelines say?

European Society for Pediatric Gastroenterology, Hepatology and Nutrition

North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition

Diagnostic Criteria

Rome III diagnostic criteria for functional constipation	
In the absence of organic pathology, >2 of the following must occur For a child with a developmental age <4 years 1. <2 defecation per week 2. At least 1 episode of incontinence per week after the acquisition of toileting skills 3. History of excessive stool retention 4. History of painful or hard bowel movements 5. Presence of a large fecal mass in the rectum 6. History of large-diameter stools that may obstruct the toilet Accompanying symptoms may indulge irritability, decreased appetite, and/or early satiety, which may disappear immediately following passage of a large stool	For a child with a developmental age >4 years with insufficient criteria for irritable bowel syndrome 1. <2 defecations in the toilet per week 2. At least 1 episode of fecal incontinence per week 3. History of retentive posturing or excessive volitional stool retention 4. History of painful or hard bowel movements 5. Presence of a large fecal mass in the rectum 6. History of large-diameter stools that may obstruct the toilet

Diagnostic Criteria

Alarm signs and symptoms in constipation	
• Constipation starting extremely early in life (<1 mo) • Passage of meconium >48 h • Constipation starting in the first month of life • Family history of Hirschsprung's disease • Ribbon stools • Blood in the stools in the absence of anal fissures • Failure to thrive • Bilious vomiting	• Severe abdominal distension • Abnormal thyroid gland • Abnormal position of the anus • Absent anal or cremasteric reflex • Decreased lower extremity strength/tone • Sacral dimple • Tuft of hair on spine • Gluteal cleft deviation • Anal scars

HD: Hirschsprung disease

Diagnosis and Management: History and Physical examinations

Some important Key pointers for FC	
Infant/toddler	**Child/adolescent**
History	History
Examination	Examination
Toilet phobia	Sexual abuse
Cystic fibrosis	Depression
Celiac disease, hypothyroidism	Cystic fibrosis
Dietary protein allergy	Celiac disease
Hirschsprung disease	Hirschsprung disease
Anatomic malformations	Spinal cord anomalies, trauma
Spinal cord anomalies	Sacral teratoma
Pseudoobstruction	Pseudoobstruction

Dosage of most frequently used oral and rectal laxatives	
Oral laxatives	**Dosages**
Osmotic laxatives Lactulose PEG 3350 PEG 4000 Milk of magnesia (magnesium hydroxide)	1-2 g/kg, once or twice/day Maintenance: 0.2-0.8 g kg^{-1} day^{-1} Fecal disimpaction: 1-1.5 g kg^{-1} day^{-1} (with a maximum of 6 consecutive days) 2-5 y: 0.4-1.2 g/day, once or divided 6-11 y: 1.2-2.4 g/day, once or divided 12-18 y: 2.4-4.8 g/day, once or divided
Fecal softeners Mineral oil	1-18 y: 1-3 mL kg^{-1} day^{-1}, once divided, max 90 mL/day
Stimulant laxatives Bisacodyl Senna Sodium picosulfate	3-10 y: 5 mg/day; >10 y: 5-10 mg/day; 2-6 y: 2.5-5 mg once or twice/day; 6-12 y: 7.5-10 mg/day; >12 y: 15-120 mg/day; 1 mo-4 y: 2.5-10 mg once/day; 4-18 y: 2.5-20 mg once/day
Rectal laxatives/enemas Bisacodyl Sodium docusate Sodium phosphate NaCl Mineral oil	2-10 y: 5 mg once/day; >10 y: 5-10 mg once/day; <10 y: 60 mL; > 6 y: 120 mL; 1-18 y: 2.5 mL/kg, max 133 mL/dose Neonate <1 kg: 5 mL, >1 kg: 10 mL; >1 y: 6 mL/kg once or twice/day 2-11 y: 30 -60 mL once/day; >11 y: 60-150 mL once/day

PEG: Polyethylene glycol

Treatment

The use of PEG with or without electrolytes orally 1 to 1.5 g /kg/ day for 3 to 6 days is recommended as the first-line treatment for children presenting with fecal impaction

In conclusion, evidence shows that PEG and enemas are equally effective for fecal disimpaction.

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, the working group decided to prefer PEG.

Treatment

The use of PEG with or without electrolytes is recommended as the first-line maintenance treatment. A starting dose of 0.4 g kg^{-1} day^{-1} is recommended and the dose should be adjusted according to the clinical response.

In conclusion, evidence shows that PEG is more effective compared with lactulose, milk of magnesia, mineral oil, or placebo.

Quality of evidence: low

Based on expert opinion, maintenance treatment should continue for at least 2 months. All symptoms of constipation symptoms should be resolved for at least 1 month before discontinuation of treatment. Treatment should be decreased gradually

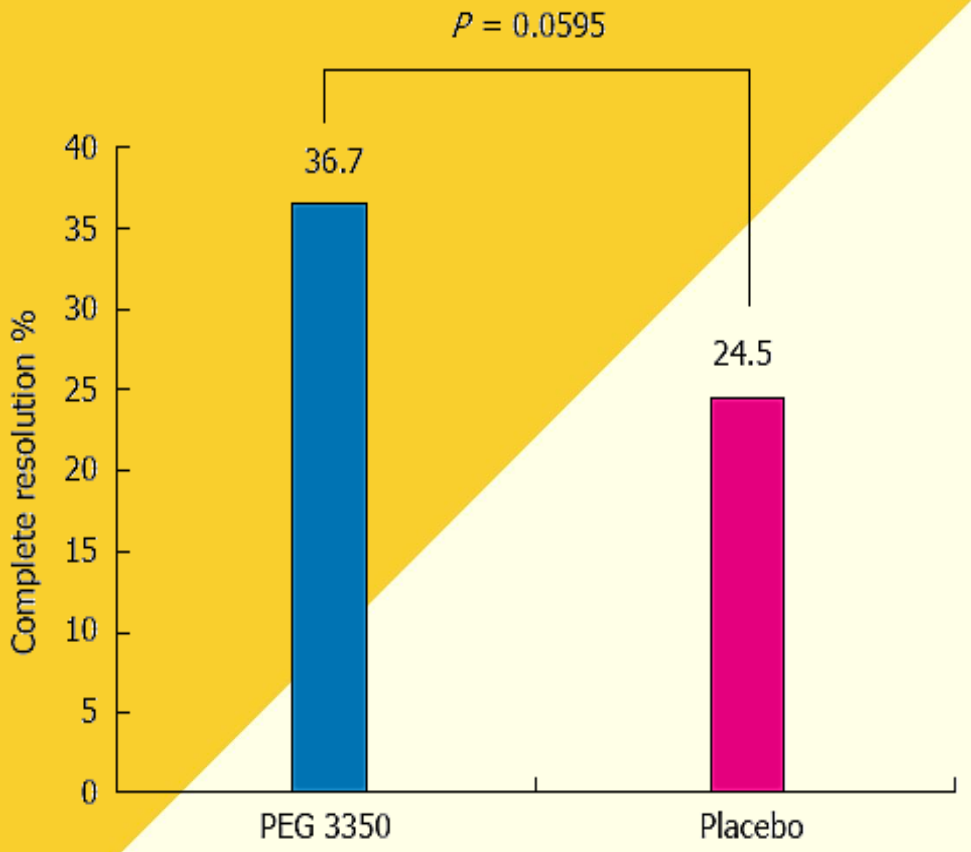
Randomized Clinical Trial

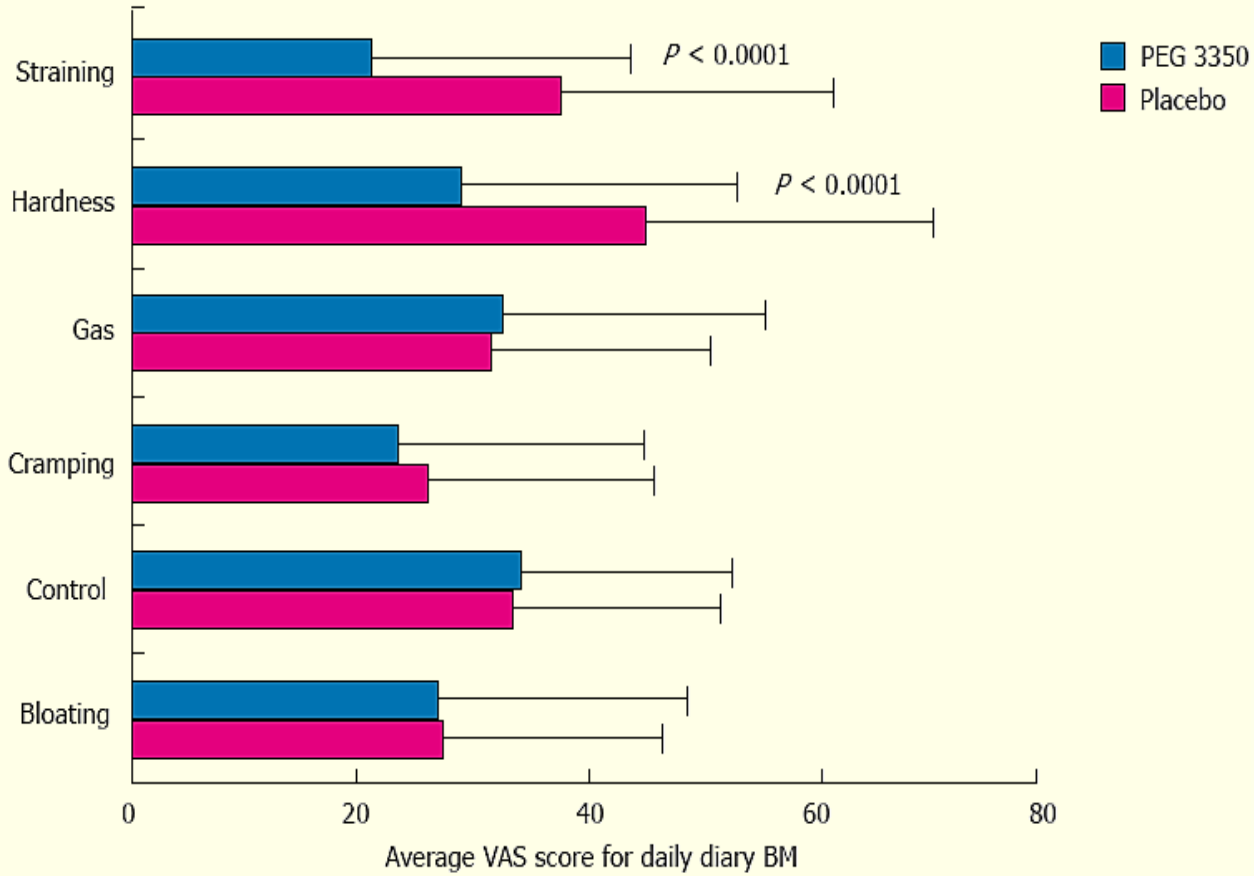
Polyethylene glycol 3350 in occasional constipation: A one-week, randomized, placebo-controlled, double-blind trial

Objective: To evaluate the efficacy and safety of polyethylene glycol (PEG) 3350 in subjects with self-reported occasional constipation.	
Methods	• ≥ 17 years of age • 203 Patients (102 in PEG Group and 101 in Placebo)
Intervention	• Placebo • PEG 3350 17g/Day – for 7 days

McGraw et al. (2016), WJGPT.

Results: Patients on PEG 3350 had more successful BMs comparing with placebo during treatment period and statistical difference achieved on day 3 of treatment.





Conclusion: PEG 3350 at a dose of 17g/day for a week, is safe, effective and well tolerated, in subjects with occasional constipation.

McGraw et al. (2016), WJGPT.

Cont..

Polyethylene Glycol Maintenance Treatment for Childhood Functional Constipation—A Randomized, Placebo-controlled Trial

*†Line Modin, †Anne Mette Walsted, *Kasper Dalby, and *Marianne Skytte Jakobsen

Objective: To investigate the long-term efficacy of polyethylene glycol (PEG) during maintenance treatment of childhood functional constipation.	
Methods	• 2-16 years of age (Rome III Criteria) • 102 patients (49 in PEG Group and 53 in Placebo)
Intervention	• Placebo (aliquots of 13.8g in plain laminate sachet) • PEG 0.8g/kg/day - for 24 weeks (dose, stool type and frequency)

Modin L et al. (2016), Clinical and experimental gastroenterology.

Results:

TABLE 2. Effect of treatment on secondary outcomes in polyethylene glycol 3350 and placebo groups

	PEG	Placebo	*P*	OR (95% CI)
Secondary outcomes				
Switched to rescue medication during the study, n (%)	2/49 (4.1)	30/53 (56.6)	<0.001	0.08 (0.02–0.35)
Weekly frequency of bowel movements at 24 wk, mean (SD)	9.1 (3.3)	8.6 (3.4)	0.46	—
Fecal incontinence at 24 wk, n (%)	14/49 (28.6)	9/53 (17.0)	0.24	1.96 (0.76–5.05)
Abdominal pain at 24 wk, n (%)	0/49	3/53 (5.7)	—	—
Additional outcomes				
Time on study medication, wk, median (p25–75)	24 (18–24)	4 (2–12)	<0.001	—
Use of study medication at 24 wk, n (%)	27/49 (55.1)	5*/53 (9.4)	<0.001	0.08 (0.03–0.25)
Believed their child received placebo†, n (%)	18/49 (36.7)	30/53 (56.6)	0.04	0.45 (0.2–0.99)

Conclusion: Maintenance treatment with PEG is significantly more effective than placebo in preventing relapse of constipation symptoms during long-term maintenance treatment in childhood FC.

Modin L et al. (2016), Clinical and experimental gastroenterology.

Clinical Trial/Experimental Study

Medicine®

OPEN

Lactulose for the treatment of Chinese children with chronic constipation

A randomized controlled trial

Yuan Cao, MB[a], Shi-ming Liu, MB[b,*]

Abstract

Background: This study aimed to investigate the efficacy and safety of lactulose for the treatment of Chinese children with chronic constipation.

Methods: A total of 100 children with chronic constipation were included in this randomized controlled trial. They were equally and randomly allocated to a treatment group (n = 50) and a placebo group (n = 50). The participants in the treatment group received lactulose, while the subjects in the placebo group received placebo intervention. The children in both groups were treated for a total of 6 weeks. The primary outcome was daily stool frequency. The secondary outcomes consisted of stool consistency, measured by the Bristol Stool Form Scale, abdominal pain, flatulence, as well as the adverse events. All outcomes were measured at baseline and after 6-weeks treatment.

Results: After 6 weeks treatment, lactulose showed better outcomes in daily stool frequency ($P < .01$), and stool consistency ($P < .01$), except the abdominal pain ($P = .24$), and flatulence ($P = .44$), compared with the placebo. Additionally, no significant differences regarding all adverse events were detected between 2 groups.

Conclusion: The results of this study found that lactulose is efficacious for Chinese children with chronic constipation after 6-weeks of treatment.

Abbreviations: ITT = intention-to-treat , SAS = statistical analysis system.

Keywords: constipation, efficacy, lactulose, safety

Results:.

Comparison stool frequency between 2 groups.

Stool frequency	Treatment group (n = 50)	Placebo group (n = 50)	*P* value
Baseline	0.6 (0.5)	0.7 (0.6)	.37
Change from baseline	0.5 (0.3, 0.8)	0.2 (0.1, 0.6)	
Difference between groups		0.4 (0.2, 0.7)	<.01

Mean ± standard deviation (range).

Comparison of stool consistency between 2 groups.

Bristol stool form scale	Treatment group (n = 50)	Placebo group (n = 50)	*P* value
Baseline	3.0 (1.1)	3.1 (1.2)	.56
Difference from treatment before	1.6 (0.9, 2.3)	0.5 (0.2, 0.9)	
Difference between groups		1.1 (0.6, 1.7)	<.01

Data are present as mean ± standard deviation (range).

Comparison of abdominal pain between 2 groups.

Abdominal pain	Treatment group (n = 50)	Placebo group (n = 50)	*P* value
Before treatment	1.6 (0.7)	1.7 (0.7)	.48
Difference from treatment before	−0.2 (−0.5, −0.1)	−0.1 (−0.3, −0.1)	
Difference between groups		−0.1 (−0.2, −0.1)	.24

Conclusion: Study found that lactulose can treat Chinese children with chronic constipation effectively and safety. Future studies with longer-term treatment and follow-up evaluation are still needed to be explored.

Cao Yet al. (2018), Medicine.

Published online 2015 May 23.

Research Article

Response and Recurrence Rate After Treatment With Polyethylene Glycol Versus Polyethylene Glycol Plus Lactulose in Children With Chronic Functional Constipation: A Randomized Controlled Trial

Saleheh Ala [1]; Mahmood Haghighat [2]; Seyed Mohsen Dehghani [3]; Hassan Bazmamoun [4,*]

Objective: The aim of this study was to investigate the response and recurrence rate after treatment with polyethylene glycol alone versus polyethylene glycol plus lactulose in children with chronic functional constipation.

Methods	• 1-12 years of age (Rome III Criteria) • 200 patients (100 in PEG (Group 1)and 100 in PEG+Lactulose (Group 2)
Intervention	• PEG (0.7 g/kg /day, 13.8 - 40 g/day), twice daily • PEG (0.7 g/kg /day, 13.8 - 40 g/day), twice daily and lactulose, maximum dose twice daily (3 cc/kg/day).

Table 2. Association Between Response Rate and Gender, Positive Family History, Mean Duration of Constipation and High Dietary Fiber [a]

Variable	Groups					
	Group 1, of 70 Improved Patients	Group 1, of 30 Without Improved Patients	P Value	Group 2, of 87 Improved Patients	Group 2, of 13 Improved Patients	P Value
Gender			0.86			0.61
Male	29 (41)	13 (43)		47 (54)	8 (61)	
Female	41 (58)	17 (56)		40 (45)	5 (38)	
Positive family history	24 (34.3)	4 (13.3)	0.32	23 (26.4)	3 (23.1)	0.79
Mean duration of constipation, mo	24.8 ± 23	32.6 ± 23.3	0.05	17.23 ± 13.2	23.9 ± 22.4	0.06
High dietary fiber	87.1 (61)	25 (83.3)	0.61	65 (74.7)	11 (84.6)	0.43

Table 3. Association Between Recurrence Rate and Gender, Positive Family History, Mean Duration of Constipation and High Dietary Fiber [a]

Variable	Groups					
	Group 1, of 58 Patients Without Recurrence	Group 1, of 11 Patients With Recurrence	P Value	Group 2, of 70 Patients Without Recurrence	Group 2, of 8 Patients With Recurrence	P Value
Gender			0.37			0.32
Male	34 (58.6)	8 (72.7)		31 (44.2)	5 (62.5)	
Female	24 (41.3)	3 (27.2)		39 (55.7)	3 (37.5)	
No Positive family history	38 (65.5)	8 (72.7)	0.64	52 (74.2)	8 (10.3)	0.96
Mean duration of constipation, mon	23.74 ± 21.64	34.27 ± 30.44	0.17	27.27 ± 23.37	36.13 ± 18.33	0.11
No high dietary fiber	7 (12)	3 (27)	0.18	14 (20)	3 (37.5)	0.25

Conclusion: There was no significant lower recurrence rate of constipation with PEG and lactulose combination therapy over PEG alone. Therefore, changing treatment from lactulose plus PEG to PEG alone would result in better compliance of patients for long-term therapy and would be cost effective.

Ala S et al. (2015), Iranian society of pediatrics.

ORIGINAL ARTICLE

Comparison of the effectiveness and safety of polyethylene glycol with and without electrolytes in the treatment of chronic constipation☆

Enrique Llerena[a,*], Vicente Varea Calderón[a], Gemma Pujol Muncunill[a], Karina Hernandez Hernandez[a], Franciso Javier Sosa Giraldo[b], Tacya Suarez Fuentes[a], Javier Martín de Carpi[a]

Objective: To compare the effectiveness and safety of polyethylene glycol with and without electrolytes (EL) over a 12 week period in treatment of chronic constipation in paediatric.	
Methods	• 1-17 years of age (Rome III Criteria) • 62patients (30 in PEG and 32 in PEG+E)
Intervention	***PEG,*** *Faecal impaction:* 1.5-2 g/kg/day in two doses until resolution for a maximum of six days (fixed dose). *Constipation:* 0.4-1 g/kg/day in two doses to a maximum of 20 g/day-12 weeks. ***PEG+E***, *Faecal impaction*: 1.5-2 g/kg/day in two doses until resolution for a maximum of six days (fixed dose). *Constipation*: 0.4---1 g/kg/day in two doses to a maximum of 27.8 g/day.

Results:

Table 3 Number of bowel movements per week.

Follow-up week	PEG + EL	PEG	*P*
6 (mean, median)	6.09 (7.00)	6.17 (7.00)	.927
12 (mean, median)	5.45 (7.00)	4.67 (4.00)	.28

Table 4 Change in stool consistency (Bristol stool scale).

Follow-up week	PEG + EL	PEG	*P*
6 (mean, median)	3.75 (4.00)	3.93 (4.00)	.3
12 (mean, median)	3.73 (4.00)	3.50 (4.00)	.61

Table 5 Electrolyte imbalances at 6 weeks.

	PEG + EL		PEG		*P*
	N	%	*N*	%	
No imbalance	14	43	5	16	.01
At least 1 in AR	18	56	25	83	.02
Only 1 in AR	9	28	10	33	.65
Only 2 in AR	5	15	14	46	.00
Only 3 in AR	3	9	1	3	.61[a]
≥4 in AR	1	3	0		1[a]

Conclusion: PEG formulations with or without EL have a quite similar effectiveness, safety and acceptability. PEG without EL produced more electrolyte abnormalities, but none of them were symptomatic.

Llerena E et al. (2016), Anales de pediatria

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Cranswick et al., Pediatr Ther 2018, 8:2
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Research Article Open Access

Polyethylene Glycols with or without Electrolytes for Constipation in Children: A Network Meta-Analysis

Noel Cranswick*, Peter Katelaris, Vasi Naganathan, John Gullotta, George Krassas and Ken Liu

Abstract

Background: Polyethylene glycol laxatives are the cornerstone of the management of constipation in children. They are available with and without electrolytes.

Aims: The aims of this network meta-analysis (NMA) were to assess the relative efficacy, safety and tolerability of polyethylene glycol with (PEG+E) or without electrolytes (PEG) in the management of constipation in children.

Methods: A systematic review and NMA was undertaken to identify and analyse all published randomised controlled clinical trials of polyethylene glycol in children with constipation. Text word searches were carried out using MEDLINE, MEDLINE in Progress, EMBASE, Cochrane Database and Systematic Reviews databases covering inception to April 2015. The primary efficacy analysis was the mean number of bowel movements per week. Secondary endpoints assessed safety, tolerability and compliance.

Results: 15 studies (involving 1,384 patients) were included in the NMA. PEG and PEG+E are both more effective than placebo, increasing the mean number of bowel movements per week by 2.3 (95% CrI 0.3, 4.4) and 2.2 (95% CrI 0.1, 4.7) respectively. Direct comparison of PEG+E with PEG identified no differences in efficacy, safety, or tolerability, with the exception of one study demonstrating better tolerability with PEG. Compared to PEG+E, PEG was easier to take, with a trend towards improved compliance.

Conclusion: This NMA provides no evidence to support the clinical utility of added electrolytes to polyethylene glycol in the management of constipation in children. PEG alone is as effective as PEG+E and both therapies are well tolerated. This analysis supports the ongoing use of polyethylene glycol as a first-line treatment of constipation in children. Formulations without electrolytes should be considered first to optimize patient acceptability and adherence.

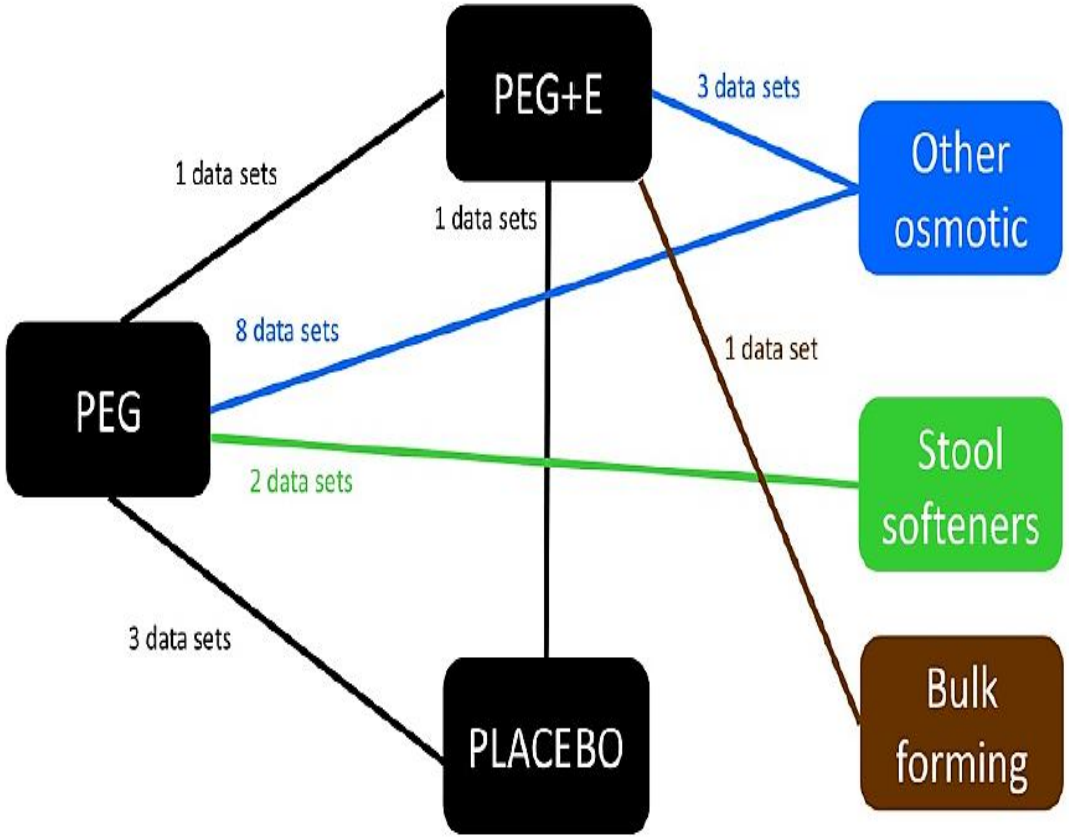
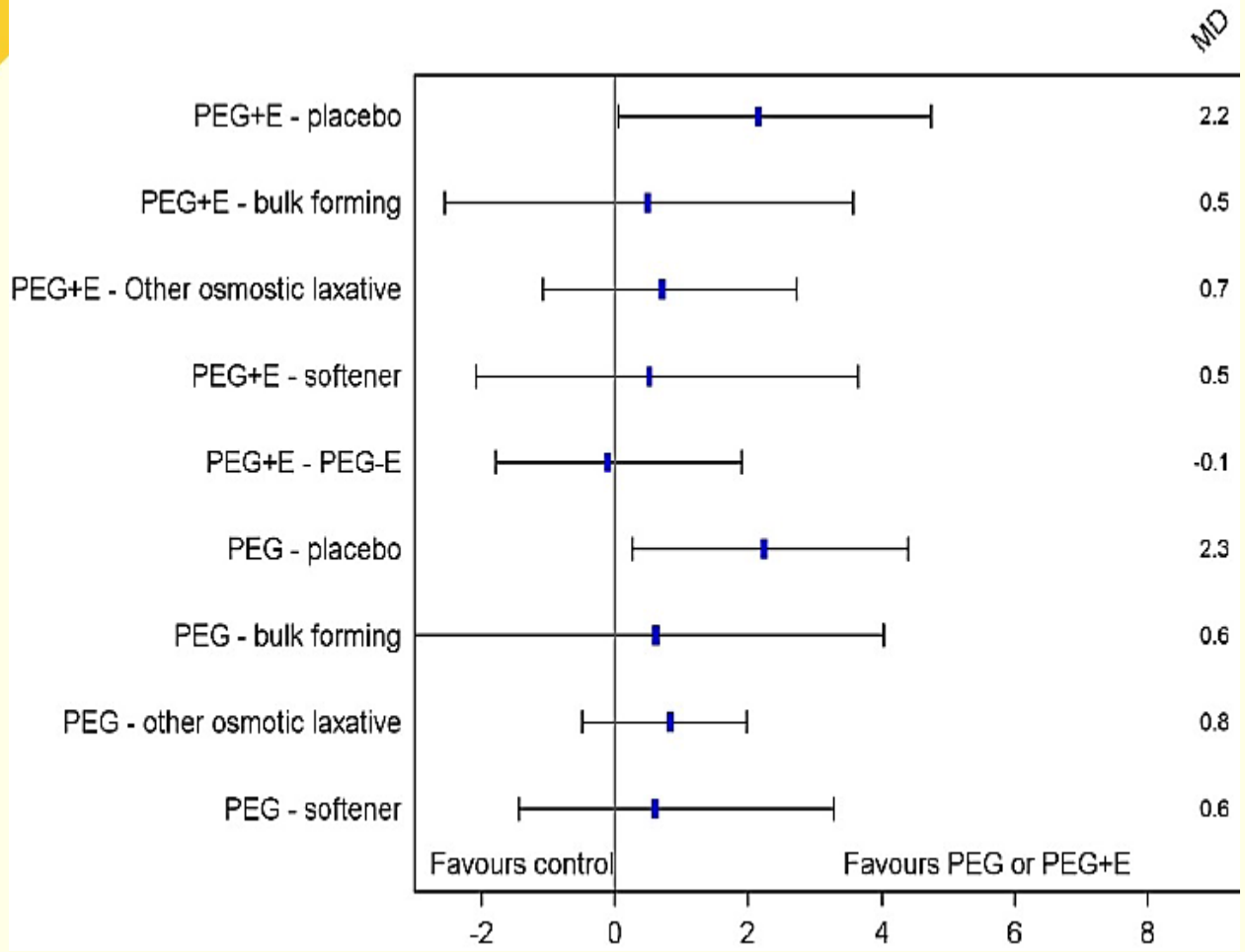


Figure 3: Network diagram, constipation treatments and direct comparisons included in the analyses (PEG=Polyethylene glycol alone, without electrolytes; PEG+E=Polyethylene glycol with electrolytes).



Both PEG and PEG+E were found to be significantly more effective than placebo.

Neol C et al. (2018), Pediatric and therapeutics

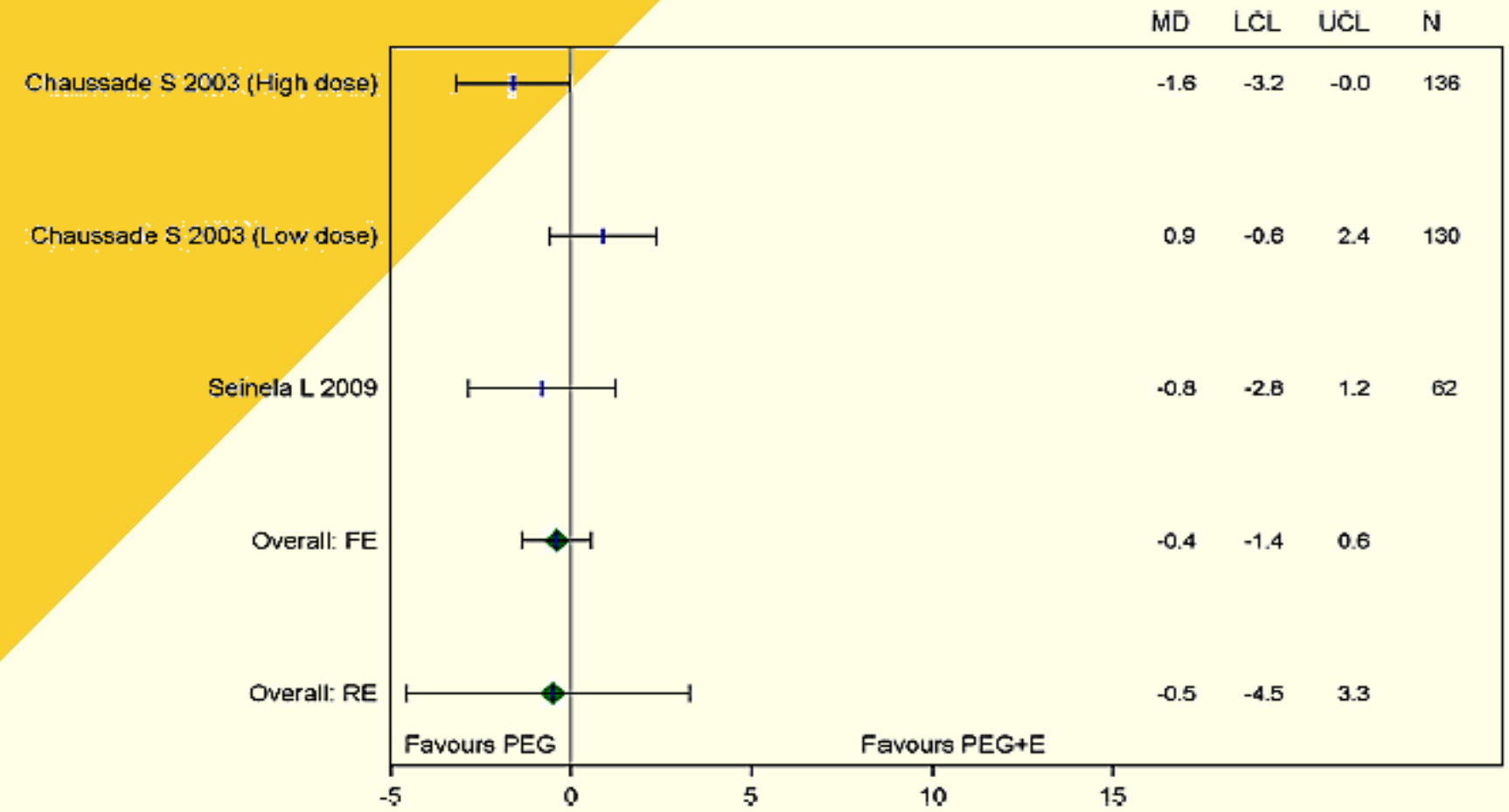


Fig. 3 Mean difference in weekly bowel movements PEG + E vs PEG (head-to-head studies)

Conclusion: Polyethylene glycol with and without electrolytes are effective and safe treatments for constipation in adults. The addition of electrolytes to polyethylene glycol does not appear to offer any clinical benefits over polyethylene glycol alone in the management of constipation.

Llerena E et al. (2016), Anales de pediatria

Effect of polyethylene glycol versus lactulose on abdominal pain in children occult constipation: a randomized controlled study

Efecto del polietilenglicol versus lactulosa sobre el dolor abdominal en el estreñimiento oculto en niños: un estudio controlado aleatorio

Mehran Hakimzadeh[1], Sayeh Mottaghi[1], Mitra Ahmadi[1], Hazhir Javaherizadeh[1,2]

[1] Dept. of Pediatric Gastroenterology, Abuzar Children's Hospital, Ahvaz Jundishapur University of Medical Sciences. Ahvaz, Iran.
[2] Alimentary Tract Research Center, Ahvaz Jundishapur University of Medical Sciences. Ahvaz, Iran.

ABSTRACT

Introduction and aim: Functional abdominal pain (FAP) is one of the major gastrointestinal complaints in childhood. Studies have reported occult constipation (OC) as one of the leading causes of abdominal pain. Recent researches have proposed laxatives as potent therapeutic targets for abdominal pain in patients with OC. However, no study has compared effect of poly ethylene glycol (PEG) and lactulose on occult constipation. **Materials and methods:** 51 patients aged 4 to 18 years with abdominal pain who had OC (defined as fecal impaction in abdominal X ray) were studied. Demographic and clinical data including age, sex, body weight, height, abdominal pain duration, abdominal pain rate and fecal odor were registered. They were randomly assigned to receive PEG (1gr/kg) or Lactulose (1cc/kg) for at least two weeks. All patients were reevaluated by pain measurement scale after at least two weeks of treatment. **Results:** It is indicated that the efficacy of PEG for reducing abdominal pain in OC was 48% while it was 37% for Lactulose. This study indicated that this efficacy is not affected significantly by sex and fecal odor, however this efficacy is influenced by age, body weight, abdominal pain duration and abdominal pain rate for both PEG and Lactulose. **Conclusion:** It could be concluded that PEG is a more efficient drug for treating abdominal pain in occult constipation than Lactulose and its optimum effect can be achieved in elder patients with more severe abdominal pain.

Keywords: *Abdominal pain; Constipation; Polyethylene glycol; Lactulose (source: MeSH NLM).*

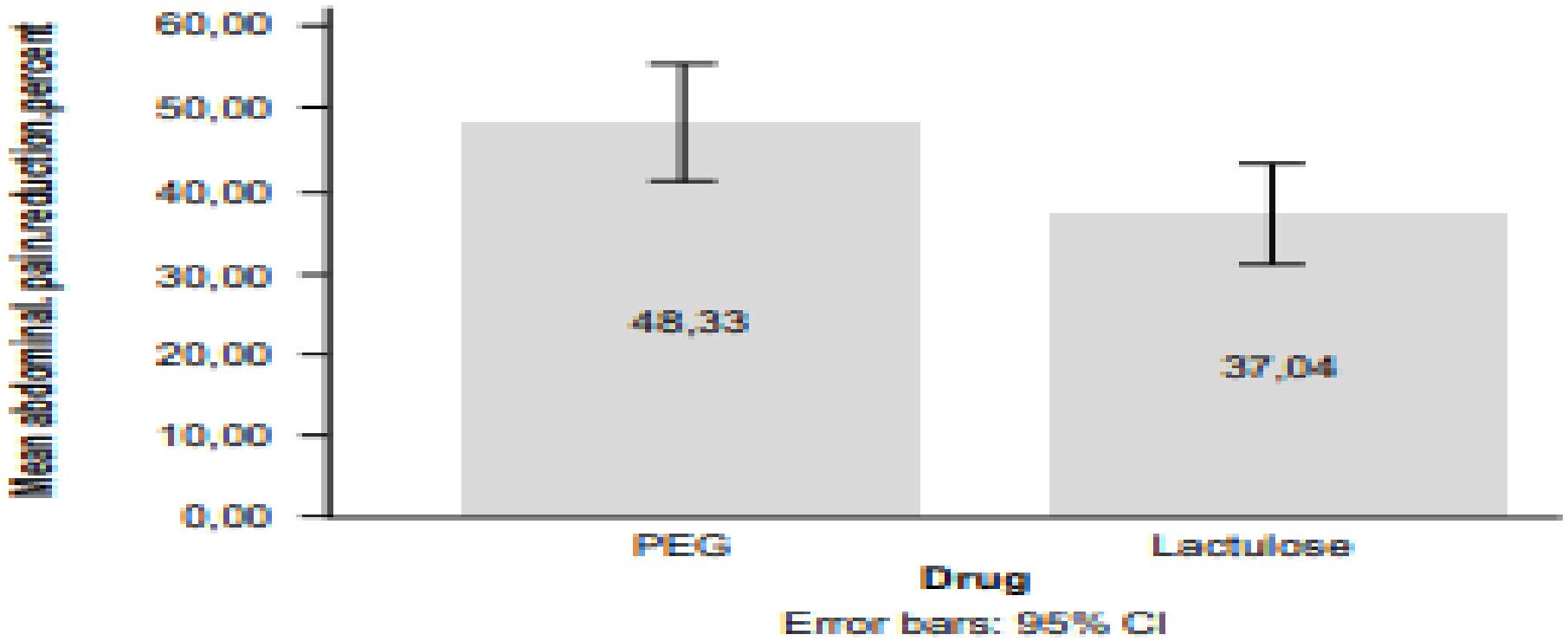


Figure 2. Comparison of PEG and lactulose efficacy in pain reduction in patients with occult constipation. Bars show percent of pain reduction which is 48.33% ± 3.44 (mean± SE) for PEG and 37.04±3.01 (mean± SE) for lactulose, the difference is significant with P value of 0.01.

J Pediatr Gastroenterol Nutr. 2019 Mar;68(3):318-324. doi: 10.1097/MPG.0000000000002192.

PEG 3350 Versus Lactulose for Treatment of Functional Constipation in Children: Randomized Study.

Jarzebicka D[1], Sieczkowska-Golub J[1], Kierkus J[1], Czubkowski P[1], Kowalczuk-Kryston M[2], Pelc M[3], Lebensztejn D[2], Korczowski B[3], Socha P[1], Oracz G[1].

Author information

Abstract

OBJECTIVES: The aim of this study was to compare the clinical efficacy and tolerance of polyethylene glycol 3350 (PEG) and lactulose for the treatment of functional constipation in infants and children.

METHODS: This randomized, multicenter study covered 12 weeks of treatment and 4 weeks of follow-up of patients with functional constipation. Patients were randomized (central randomization) to receive either PEG or lactulose. The primary end points were the number of defecations per week after 12 weeks of treatment and improvement in stool consistency of at least 2 points in the Bristol scale. The secondary end point was the presence of adverse events. Bowel movements ≥3 per week and stool consistency ≥2 (Bristol scale) were considered as successful treatment.

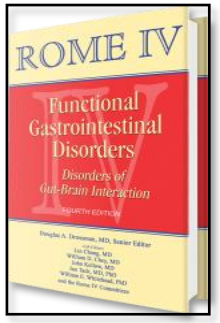
RESULTS: We enrolled 102 patients (M 57, F 45) aged 3.62±1.42 years and 88 completed the study. At week 12, good clinical outcome was achieved in 98% (PEG) and 90% (lactulose). The PEG group had more defecations per week compared with the lactulose group (7.9±0.6 vs 5.7±0.5, P=0.008) and both groups had similar frequency of defecation with pain (5% vs 5%, P=0.9), stool retention (7% vs 10%, P=057), large volume of stools (30% vs 31%, P=0.9) and hard stools (7% vs 13%, P=0.58). There were more patients with side effects in the lactulose group (15 vs 23, P=0.02), mostly bloating and abdominal pain.

CONCLUSIONS: PEG 3350 is more effective and causes fewer side effects than lactulose in the treatment of constipation in infants and children.

TRIAL REGISTRATION: ClinicalTrials.gov NCT03177434.

Importance of PEG in Functional Constipation

PEG is recommended by ISPGHAN and IAP for Disimpaction and maintenance therapy of FC in children



PEG is the first-line therapy for constipated children as per ROME IV criteria

PEG with or without electrolytes is recommended as the first-line treatment for children presenting with fecal impaction and as maintenance therapy as per ESPGHAN and NASPGHAN guidelines

Summary

- **Functional Constipation is an underestimated but common health problem worldwide, decreasing the quality of life**
- In the last decade, significant progress had been made in understanding the pathophysiology and treatment of childhood constipation
- Functional constipation should be diagnosed in the absence of red flags
- Impacted (incontinent) and non-impacted subgroups should be identified
- Management protocol should be adapted as per the algorithm suggested by the National and International Society guidelines
- Emphasis should be laid on toilet-training and importantly in counseling particularly related to long-term usage of medical therapy
- **PEG is the first line of therapy for Functional Constipation in children as suggested by the ISPGHAN and IAP, ROME IV criteria and ESPGHAN and NASPGHAN guidelines**


THANK YOU
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THE WALK TO CURE DIABETES
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We're on Track For a Cure