Is polyethylene glycol safe and effective for chronic constipation in children?

Report by
R Arora, R Srinivasan, *Llandough Hospital, Cardiff, UK; reemaraman@doctors.org.uk*
doi: 10.1136/adc.2005.072918

Chronic constipation is a frequently encountered problem in the paediatric wards and clinics. Your usual line of management has been to prescribe adequate doses of regular lactulose and use sodium picosulphate as a second line laxative or as add on treatment. Recently, you have become aware of a new drug—polyethylene glycol (PEG). As you have not prescribed this drug earlier, you want to appraise the evidence before using it in your clinical practice.

Structured clinical question

In children with chronic constipation [patients] is polyethylene glycol [intervention] better in improving stool frequency and consistency [outcome] while causing fewer side effects?

Search strategy and outcome

Primary sources

Medline via Pubmed: Search was done using headings ''Child''[MeSH] AND ''Polyethylene Glycols''[MeSH] AND (''Constipation''[MeSH] OR ''Fecal Impaction''[MeSH]). Twenty articles were found of which eight were relevant.

To find articles that had been published but were still waiting to be indexed, another search was carried out with the terms ''polyethylene glycol AND constipation AND child*''. Two further relevant articles were found.

Proceedings of major meetings: The abstract of one relevant unpublished article was also included which was presented at the 2nd World Congress of Pediatric Gastroenterology, Hepatology and Nutrition in Paris in 2004 after contacting the author and obtaining additional information.

Secondary sources

Cochrane database, BestBets: No papers found.

Summary

See table 1.

Commentary

Chronic constipation in children is a common gastrointestinal disorder encountered in general paediatric clinics and forms a substantial part of the paediatric gastroenterologist's workload. The majority of constipated children have functional constipation and despite laxative use, success is modest. Management options include a combination of healthy eating aimed at increasing fibre and fluid intake, regular toileting, reinforcement with appropriate rewards, and laxative therapy. Combining laxative use with behavioural therapy has been shown to be better than laxative use alone.[12] A high level of motivation and perseverance are necessary for these measures to be successful, and hence a continued search for a better laxative in terms of efficacy, safety, and compliance continues.

High dose PEG with electrolytes has been available for intestinal lavage preceding radiological and surgical procedures in children for some time. The electrolytes are added to prevent their loss through the faeces due to the large volume of the lavage, but this gives the lavage solution an unpleasant salty taste. A low dose version, such as PEG 3350, is available with electrolytes (in the UK and Netherlands) or without electrolytes (in the USA); it has been in commercial use only in the last few years and is used in much smaller volumes. It has been classed as an iso-osmotic laxative and acts by opposing absorption of water from faecal material in the large bowel and thus retaining water in the faeces, which is different from the laxatives such as lactulose which draw fluid from the body into the bowel lumen due to its high osmotic load.[13] PEG is physiologically inert and is not absorbed or metabolised in the gut, giving it an unlimited ''ceiling of action''.[13]

From the available evidence it is clear that PEG is effective for both disimpaction and maintenance in children of all age groups with chronic constipation. The compliance with PEG treatment is high. In the controlled studies,[1–4] PEG has been shown to be more effective than a placebo and lactulose, and at least as effective as milk of magnesia, with a much higher compliance than any of the others. It seems safe with or without added electrolytes. Only one of the above studies actually assessed the serum electrolyte levels post-treatment; abnormal levels were not found.[10] Literature search did not reveal any case reports of adverse effects to the use of low dose PEG 3350 with or without electrolytes.

There are still some unresolved questions such as the issue of adding electrolytes, the most effective molecular weight of PEG (PEG 3350 *v* PEG 4000), and the safety profile of the drug in all age groups. The drug appears promising, and though its use at present is mainly in those with inadequate response to other laxatives, it is increasingly being used as first line treatment.

CLINICAL BOTTOM LINE

- Low dose PEG is effective, both in the short and long term management of constipation in children.
- Low dose PEG with or without added electrolytes is safe in the treatment of constipation in children.
- More studies are needed to determine the most safe and effective form of PEG in children.

REFERENCES

1 **Voskuijl W,** de Lorijn F, Verwijs W, *et al.* PEG 3350 (Transipeg) versus lactulose in the treatment of childhood functional constipation: a double blind, randomised, controlled, multicentre trial. *Gut* 2004;**53**:1590–4.
2 **Thomson M.** A placebo controlled crossover study of movicol in the treatment of childhood constipation. *J Pediatr Gastroenterol Nutr* 2004;**39**(suppl 1): S16.
3 **Gremse DA,** Hixon J, Crutchfield A. Comparison of polyethylene glycol 3350 and lactulose for treatment of chronic constipation in children. *Clin Pediatr (Phila)* 2002;**41**:225–9.
4 **Youssef NN,** Peters JM, Henderson W, *et al.* Dose response of PEG 3350 for the treatment of childhood fecal impaction. *J Pediatr* 2002;**141**: 410–14.
5 **Loening-Baucke V.** Polyethylene glycol without electrolytes for children with constipation and encopresis. *J Pediatr Gastroenterol Nutr* 2002;**34**: 372–7.
6 **Loening-Baucke V,** Krishna R Pashankar DS. Polyethylene glycol 3350 without electrolytes for the treatment of functional constipation in infants and toddlers. *J Pediatr Gastroenterol Nutr* 2004;**39**:536–9.
7 **Michail S,** Gendy E, Preud'Homme D, *et al.* Polyethylene glycol for constipation in children younger than eighteen months old. *J Pediatr Gastroenterol Nutr* 2004;**39**:197–9.
8 **Pashankar DS,** Bishop WP, Loening-Baucke V. Long-term efficacy of polyethylene glycol 3350 for the treatment of chronic constipation in children with and without encopresis. *Clin Pediatr (Phila)* 2003;**42**:815–19.
9 **Erickson BA,** Austin JC, Cooper CS, *et al.* Polyethylene glycol 3350 for constipation in children with dysfunctional elimination. *J Urol* 2003;**170**(4 pt 2):1518–20.
10 **Pashankar DS,** Loening-Baucke V, Bishop WP. Safety of polyethylene glycol 3350 for the treatment of chronic constipation in children. *Arch Pediatr Adolesc Med* 2003;**157**:661–4.

Table 1 Polyethylene glycol in constipation

Citation, country	Study group	Study type (level of evidence)	Outcome	Key results	Comments
Voskuijl *et al* (2004), Netherlands[1]	100 children (6 months–15 years) with constipation received PEG 3350 or lactulose for 8 weeks. They were then asked to continue in an open-label assessment for an additional 18 weeks. 91 completed the study	Multicentre, double blind RCT. (level 1b)	Clinical efficacy at 8 weeks	Significant increase in the mean defecation frequency/week and a significant decrease in the mean encopresis frequency/week were found in both groups. 56% (95% CI 39–70) in PEG group were successfully treated compared to 29% (95% CI 16–44) in lactulose group	Used PEG 3350 (with electrolytes) in lower doses than used in other studies
			Adverse effects	No serious adverse effects recorded. Those taking lactulose reported significantly more adverse events like flatulence	
Thomson (2004), UK[2]	51 children aged 2–11 years (mean 5 y) entered a double blind treatment phase and were randomised to receive either PEG 3350 or matching placebo for first 2 weeks. After a 2 week washout period cross-over to receive alternative treatment was done for another 2 weeks	Double blind RCT with crossover (level 1b)	Stool frequency	Mean 3.59/week in PEG group *v* 1.58/week in placebo group ($p<0.001$) after first 2 weeks	Used PEG with electrolytes. Adequate wash-out before cross-over. Presented at WCPGHAN 2004. Unpublished as yet. Details through personal communication
			Soiling events	Mean 4.65/week in PEG group *v* 4.7/week in control group ($p=0.685$)	
			Symptoms	Pain on defecation, straining on defecation and stool consistency significantly better on PEG. Abdominal pain similar in both groups	
			Adverse effects	Frequency of adverse effects similar to placebo	
Gremse *et al* (2002), USA[3]	37 patients aged 2 to 16 years with constipation received either PEG 3350 or lactulose for 2 weeks followed by the other agent for 2 weeks as part of an unblinded, randomised, crossover design	RCT with crossover (level 1b)	Stool frequency	Increased from 1.7 ± 0.8/wk to 14.8 ± 1.4/wk for PEG 3350 and 13.5 ± 1.5/wk for lactulose	No wash out period during crossover
			Stool consistency and ease of passage	Similar for both laxatives	
			Colonic transit time	Total transit time was 47.6 ± 2.7 h (mean $\pm$SE) for PEG 3350 and 55.3 ± 2.4 h for lactulose ($p=0.038$)	
			Palatability and efficacy (as reported by child and parent)	PEG 3350 was effective in 31/37 patients (84%; 95%CI 68%–94%) and lactulose was effective in 17/37 (46%; 95%CI 30%–63%) ($p=0.002$). PEG 3350 was preferred by 27/37 respondents (73%) compared to lactulose	
Youssef *et al* (2002), USA[4]	4 doses of PEG 3350: 0.25 g/kg/day, 0.5 g/kg/day, 1 g/kg/day, and 1.5 g/kg/day were given for 3 days in 41 children with constipation for >3 months and evidence of faecal impaction	Individual double blind RCT (level 1b)	Disimpaction	Disimpaction achieved in 30 children (75%). 95% of higher dose patients (1–1.5 g/kg/day) achieved disimpaction *v* 55% of low dose patients (0.25–0.5 g/kg/day)	Demonstrated the use of PEG 3350 for disimpaction and dose response relation
			Symptoms	Less straining and looser consistency was noticed with increasing doses, with no statistically significant difference noted between the dose groups in any of the stool characteristics	
			Adverse effects	Diarrhoea and bloating was more common in higher dose group. No patient had clinically significant abnormal laboratory values	
Loening-Baucke (2002), USA[5]	28 children with constipation treated with PEG (0.5–1 g/kg/day) were compared with 21 children treated with milk of magnesia (1–2.5 ml/kg/day)	Individual case- control study (level 3b)	Efficacy	On 3 monthly follow ups for a year, bowel movement frequency increased and soiling frequency decreased significantly in both groups. But compared to children on milk of magnesia those on PEG were soiling more frequently ($p<0.01$) and fewer had improved ($p<0.01$) at the 1 month follow up. This difference disappeared at subsequent follow ups	Not randomised. Demonstrated a high level of compliance to PEG
			Side effects	More diarrhoea seen in PEG group but no dehydration	
			Compliance	None refused PEG whereas 33% refused to take milk of magnesia	

Table 1 Continued

Citation, country	Study group	Study type (level of evidence)	Outcome	Key results	Comments
Loening-Baucke *et al* (2004), USA[6]	75 children from age 1–24 months (mean age 17 mth) with constipation were started on PEG; average dose of 1 g/kg/day	Case series (level 4)	Stool frequency	Increased from 3.7±3.2/wk to 12.4±7.0/wk in the initial 4 months and then 8.6±3.1/wk over long term. Also significant improvement in signs and symptoms of constipation. Constipation relieved in 85% with short-term and 91% with long-term therapy	Demonstrated the efficacy, tolerability and safety of PEG use for constipation in <2 year olds
			Effective dose	Average effective dose was 1.1 g/kg/day over short term and 0.8 g/kg/day over long term	
			Adverse effects	5 had diarrhoea which improved on decreasing the dose. PEG was not stopped in anyone	
Michail *et al* (2004), USA[7]	28 patients younger than 18 months (range 7 weeks to 17 months) with constipation were started on PEG and mean duration of therapy was 6.2±5 months	Case series (level 4)	Dose	Mean initial dose was 0.88 kg/day Mean effective maintenance dose was 0.78 kg/day	Demonstrated the efficacy, tolerability and safety of PEG use for constipation in <18 month olds
			Efficacy	Mean stool frequency increased from 2.2±0.1/wk to 8.4±2.5/wk ($p<0.001$). Mean stool consistency score increased from 1.7±0.5 to 3.8±0.8 ($p<0.001$). PEG relieved constipation in 97.6% of patients	
			Side effects	1 (3.6%) infant had flatulence and 4 (14.3%) had transient diarrhoea which resolved after dose adjustment	
Pashankar *et al* (2003), USA[8]	74 children with chronic constipation (31 also had encopresis) were given PEG for 3–30 mth (mean 8.4 mth) to assess long-term efficacy	Case series (level 4)	Efficacy in constipation	Average dose 0.78 g/kg/day. Stool frequency increased from 2.9±0.3/wk to 9.9±0.7/wk ($p<0.001$). Stool consistency score (from 1 to 5) increased from 1.4±0.1 to 3.1±0.1 ($p<0.001$). Also significant improvement in signs and symptoms of constipation. Good daily compliance in 93%	Efficacy and compliance over long term was studied
			Efficacy in constipation and encopresis	Average dose 0.69 g/kg/day. Stool frequency increased from 3.0±0.5/wk to 12.5±1.5/wk ($p<0.001$). Stool consistency score (from 1 to 5) increased from 1.4±0.1 to 3.1±0.1 ($p<0.001$). Soiling events decreased from 11.0±1.6/wk to 1.8±0.5/wk ($p<0.001$). Also significant improvement in signs and symptoms of constipation. Good daily compliance in 90%	
Erickson *et al* (2003), USA[9]	46 children with constipation and dysfunctional voiding were given PEG 3350 to evaluate efficacy, compliance and side-effects	Case series (level 4)	Stool frequency	Increased from 0.42±0.2/day to 1.25±0.42/day ($p=0.0001$)	Addressed efficacy in those with constipation and resulting disorders in micturition
			Dysfunctional voiding	18 (39%) children became dry, 26 (56.5%) had decreased wetting and 2 showed no improvement	
			Voided volume	Increased from 146 ml to 210 ml ($p<0.0001$)	
			Post-void residual volume	Post-void residual volume decreased from 92 ml to 48 ml ($p<0.0001$)	
			Side effects	9/46 had diarrhoea and 1 stopped treatment	
Pashankar *et al* (2003), USA[10]	83 children (>2 y) with chronic constipation (39 also had encopresis) were given PEG for 3–30 mth (mean 8.7 mth) to assess safety profile of long-term therapy	Case series (level 4)	Clinical adverse effects	Dose-related diarrhoea in 10%, flatulence and bloating in 6% and abdominal pain in 2%	Long-term compliance and safety for PEG studied Transient liver enzyme elevation not seen in subsequent studies
			Biochemical changes	Nine subjects had transient mild elevation in ALT and 3 in AST which self-corrected in 11 later. Thought to be unrelated to PEG	
			Patient acceptance	Good daily compliance in 90%. Caretaker reported improvement in 91% and liked by 73% of children	

Table 1 Continued

Citation, country	Study group	Study type (level of evidence)	Outcome	Key results	Comments
Pashankar and Bishop (2001), USA[11]	24 children (18 mth–12 y) with chronic constipation (with/without soiling) were started on 1 g/kg/day of PEG (dose adjusted subsequently) for a total of 8 weeks	Case series (level 4)	Stool frequency	Increased from 2.3±0.4/wk to 16.9±1.6/wk ($p<0.0001$)	Open labelled trial
			Stool consistency	Score (from 1 to 5) increased from 1.2±0.1 to 3.3±0.1 ($p<.0001$)	No controls
			Soiling events (9 children)	Decreased from 10.0±2.4/wk to 1.3±0.7/wk ($p=0.003$)	
			Optimal dose	Range 0.27–1.42 g/kg/day (mean 0.84 g/kg/day)	
			Tolerance	No significant adverse effects besides dose related diarrhoea. No subject discontinued treatment	

11 **Pashankar DS,** Bishop WP. Efficacy and optimal dose of daily polyethylene glycol 3350 for treatment of constipation and encopresis in children. *J Pediatr* 2001;**139**:428–32.
12 **Baker SS,** Liptak GS, Colletti RB, *et al.* Constipation in infants and children: evaluation and treatment. A medical position statement of the North American Society for Pediatric Gastroenterology and Nutrition. *J Pediatr Gastroenterol Nutr* 1999;**29**:612–26 (erratum: *J Pediatr Gastroenterol Nutr* 2000;**30**:109.
13 **Ungar A.** Movicol in treatment of constipation and faecal impaction. *Hosp Med* 2000;**61**:37–40.

Are antiemetics helpful in young children suffering from acute viral gastroenteritis?

Report by
S M Borowitz, *Division of Pediatric Gastroenterology, University of Virginia, Charlottesville, Virginia 22908, USA; Witz@virginia.edu*

doi: 10.1136/adc.2004.064972

An 18 month old female is brought to the emergency department by her mother. She has been suffering from repeated vomiting and diarrhoea for the past 24 hours. Over the past eight hours she has vomited approximately 12 times. The vomitus has not contained any bile or blood. The little girl appears mildly dehydrated. Her stool tests positive for rotavirus. You wonder whether administration of an antiemetic may lessen her symptoms and increase the likelihood that oral rehydration therapy will be successful.

Structured clinical question
In an 18 month old girl with rotavirus gastroenteritis [patient], does the administration of antiemetic medication [intervention] decrease vomiting and increase the likelihood that oral rehydration therapy will be successful [outcome]?

Search strategy and outcome
Secondary sources: none.

Medline 1966–July, 2004 using OVID interface: ondansetron OR promethazine OR metoclopramide OR antiemetics AND exp rotavirus infections OR exp Norwalk virus OR exp gastroenteritis OR exp enteritis OR exp transmissible gastroenteritis virus OR exp rotavirus

Limits: human, English language, all infant (birth to 23 months) or preschool child (2 to 5 years) or child (6 to 12 years).

No systematic reviews. Seventy papers were identified, four of which were relevant.

See table 2.

Commentary
No study expressly answered the question as to whether antiemetics lessen the vomiting associated specifically with rotavirus gastroenteritis infection in children and increase the likelihood that oral rehydration therapy will be successful. In the one study in which the authors attempted to identify the cause of gastroenteritis,[3] approximately half of the enrolled children were suffering from rotavirus gastroenteritis. It is reasonable to assume that at least similar numbers of children in the other studies were suffering from rotavirus infection.

In one study,[2] oral ondansetron (1.6–4 mg/dose depending on the child's age) or placebo was administered in the emergency department and then every eight hours for up to two days. Compared to the controls, children that received ondansetron experienced less vomiting while they were in the emergency department, were less likely to require intravenous fluid therapy, and were less likely to be admitted to the hospital. In another study,[1] a single dose of intravenous ondansetron (0.15 mg/kg) or placebo was given in the emergency department. All of the children in this study also received intravenous fluids. The children who received ondansetron had significantly less vomiting in the emergency department than did the children who received placebo. Hospitalisation rates were comparable in the two groups; however when the authors excluded children who had a serum CO_2 less than 14 mEq/l or had received intravenous fluids prior to their emergency room visit, those who received ondansetron were significantly less likely to be admitted to the hospital than were children who were treated with placebo.

Cubeddu and colleagues[3]showed that in children hospitalised with gastroenteritis, a single dose of intravenous ondansetron (0.3 mg/kg) decreased the frequency of vomiting over the subsequent 24 hours compared to a single dose of metoclopramide (0.3 mg/kg) or placebo. Van Egan and colleagues[4] showed that in children hospitalised with gastroenteritis, 30 mg domperidone suppositories decreased the amount of vomiting compared 10 mg metoclopramide suppositories or placebo. In both of these two studies, metoclopramide was not superior to placebo.

In these four studies comprising 358 patients, no serious side effects were associated with the administration of