

Review Article

Supplementary Table 1: Details of randomised controlled trials and open label studies.

Study	N	Intervention group		Duration of	Effectiveness mean weekly stool frequency		Other outcomes	Results	Safety	Conclusion	
					Baseline	End of the treatment	-				
Voskuijl, et al. [15]	100	PEG 3350	Lactulose	8 weeks	PEG-2.5 Lactulose-2.75	PEG-7.12 (P value<0.01) Lactulose-6.43 (P<0.01)	1.Successful treatment 2.encopresis frequency	PEG 56% vs lactulose 29 % (P=0.02) PEG-before treatment 9.7 vs after treatment 3.1 (<0.01) Lactulose-before treatment 7.7 vs after 2.8 treatment (<0.01)	Abdominal pain, bloating diarrhea flatulence, vomiting straining, and pain at defecation are reported more in the lactulose group than in children using PEG	PEG 3350 compared with lactulose provided a higher success rate with fewer side effects.	
Rafati, et al. [16]	160	PEG 3350	Liquid parafin	4 months	PEG-1.6 Liquid paraffin-1.4	PEG-8.7-significant Liquid paraffin-7.5- significant	Treatment success	PEG-95% vs liquid paraffin 87% (P=0.087).	Adverse reactions like nausea, vomiting, flatulence, abdominal pain and dehydration, occurred more frequently in patients using liquid paraffin compared with PEG 3350	PEG 3350 was as effective as liquid paraffin but with fewer adverse drug events.	
Modin et al. [17]	102	PEG 3350	Placebo	24 weeks	PEG-5.4 Placebo-5.2	PEG-9.1 Placebo-8.6	PEG-9.11.Treatment successPEG-67% vs 36% in placebo-significantAbdominal pain and were the most com complaint which wa serious adverse ev placebo-8.6Abdominal pain and were the most com complaint which wa serious adverse ev related to the study were not report		Abdominal pain and fever were the most common complaint which was seen. serious adverse events related to the study drug were not reported	Maintenance treatment with PEG is significantly more effective than placebo in preventing relapse of constipation symptoms during long- term maintenance treatment in childhood FC.	

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Bulk laxatives	38	polyethylene glycol 4000	magnesium hydroxide	6 months	PEG-2 magnesium hydroxid-1.33	PEG-5.75 magnesium hydroxid-4.9	 1.stool consistency-4 or 5 stools scale 2.faecal incontinence 3.abdominal pain 4.straining 5.PEG acceptance 	PEG-80% vs mg (0h)2- 75 % (P=0.217) PEG-6.6% vs mg (0h)2-0% (P=0.362) Peg-20 vs mg (0h)2- 16% (P=0.825) PEG-0 mg (0h)2-8.3% (P=0.255) PEG-91.6% vs mg (0h)2-33.3% P	NA	The two laxatives showed no difference in effectiveness for the treatment of constipation. However, due to its better acceptance, because it is odourless and tasteless, polyethylene glycol proved to be a better option for treating chronic functional constipation
Kokke, et al. [19]	147	fiber mixturec	lactulose	8 weeks	fibre mixture-3 Lactulose-2	fibre mixture 7 Lactulose-6	1.Consistency of stools (BSFS) 2.Faecal incontinence (1 or more episodes/week)	Fibre-3.6 vs lactulose 4.0 (P=0.01) Fiber-9 patients vs lactulose-5 patients (P=0.008)	Abdominal pain and flatulence scores were similar in both groups. No serious adverse effects were registered.	A fluid fibre mixture and lactulose give comparable results in the treatment of childhood
Farahmand, et al. [20]	247	Liquid paraffin	Lactulose	8 weeks	Liquid paraffin-1.6 Lactulose-1.8	Liquid paraffin-13.1 Lactulose-8.1	1.Encopresis frequency/week 2.Treatment success	liquid paraffin-0 vs lactulose-3 (P<0.001) Liquid paraffin group (85%) vs lactulose (29%) (P<0.001)	There were no serious or significant adverse events recorded during 8 weeks of treatment in both groups. However significantly more adverse events were reported by patients using lactulose compared with patients on liquid paraffin	Liquid paraffin is more effective than lactulose in the treatment of chronic functional constipation in children
Dupont, et al. [21]	96	PEG 4000	Lactulose	3 months	PEG-6 Lactulose-7	PEG-7 Lactulose-6	 1.stool consistency- hard stools 2.Faecal impaction 3.use of additional laxatives - enemas 	PEG-6% vs lactulose-28% (P=0.008) PEG-2% vs lactulose-13 % (P=0.049). 17% PEG vs 41% lactulose (P=0.012)	Biological tolerance was similar between both groups Clinical tolerance was similar for both treatments except for vomiting and flatulence, which were significantly higher with lactulose.	Peg is similar or more effective than lactulose and long-term tolerance is more in PEG.

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Jarzebicka, et al. [22]	102	PEG 3350	Lactulose	12 weeks	PEG-2.19 Lactulose-2.08	PEG-7.9 Lactulose-5.7	1.frequency of defecation with pain 2.stool retention 3.large volume of stools 4.hard stools -	PEG-5% vs lactulose-5% (P=0.99) PEG-7% vs lactulose-10% (P=0.70) PEG-30% vs lactulose-31% (P=0.99) PEG-7% vs lactulose-13% (P=0.46)	More side effects were observed in the lactulose groups like bloating and abdominal pain, when compared to the PEG group (P=0.02), which is significant.	PEG 3350 is more effective and causes fewer side effects than lactulose in the treatment of constipation in infants and children
Karami, et al. [23]	126	PEG	Liquid paraffin	2 weeks to 12 months	PEG-2.6 4.7 Liquid	PEG-4.7 (P=0.001) Liquid paraffin-4.5	1.Stool consistency 2.painful defecation	PEG-4.1 pre-treatment us 4.7 after treatment (P=0.001) Liquid paraffin-4.1 pre-treatment us 4.5 after treatment (P=0.001) PEG-1.3 pre-treatment us 1.9 after treatment (P=0.001) Liquid paraffin-1.3 pre-treatment us	NA	PEG is more effective than oral liquid paraffin for the treatment of childhood functional constipation
					paraffin-3.0	(P=0.001)	3.encopresis	PEG-3.2 pre-treatment (P=0.001) PEG-3.2 pre-treatment vs 3.8 after treatment (P=0.001) Liquid paraffin-3.4 vs 3.8 after treatment (P=0.001)		
							1.Asymptomatic	PMF-100-77% vs 20% placebo (P<0.01)		
Corazziari, et al. [24]			Placebo	12 weeks	PMF 100-1.5	PMF 100-7.4	2.straining at defecation	PMF-100-22% vs 49% placebo (P<0.001)	Adverse events, including gastrointestinal and extra	Administration of small daily doses of isosmotic PEG electrolyte balanced
	70	PMF-100			Placebo-1.29	Placebo-4.3	3.hard stools	PMF-100-4% vs 27% placebo (P<0.001)	gastrointestinal symptoms were not significantly different between groups	solutions was effective over a six-month period for the treatment of functional
							4.completion of trials	PMF-100-70% vs 31% placebo (P<0.001)		constipation

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Llerena, et al. [25]	62	PEG+E PEC	G 12 weeks	PEG+E-1.66 PEG-1.63	PEG+E-5.4 PEG-4.6	1.Stool consistency (BSC)	PEG+E-3.7 vs PEG-3.5 (P=0.6)	None of the patients had abnormal results in the complete blood count, total serum protein, albumin, or transaminase levels Mild Hyponatremia was found in 15% of the PEG+E group compared to 36 % in the PEG group. (P=0.05)	PEG formulations with or without EL have quite similar effectiveness, safety, and acceptability.
Urganci, et al. [26]	40	Liquid paraffin Lactul	ose 8 WEEKS	Liquid paraffin-1.1 Lactulose-1.2 (P<0.05	Liquid paraffin - 16.1 Lactulose-12.3 (P<0.05)	1.stool consistency 2.compliance	Liquid paraffin-29 vs lactulose-2.21 (>0.05) Liquid paraffin-90 vs lactulose 60 (P=0.02)	Adverse events like vomiting, bloating and increased flatulence, and abdominal cramping was seen in both groups. But liquid paraffin was better tolerated, and compliance was higher compared with the lactulose	Patients treated with liquid paraffin responded more rapidly than patients responding with lactulose and showed fewer side- effects.
Gondo, et al. [27]	39	PEG 3350+E	12 weeks	1	5.18 (P<0.001)	1.weekly stool consistency 2.Proportion of children used rescue medication	Pre-treatment -2.4 vs after treatment -4.4 Pre-treatment -77% vs after treatment-0%	3 mild adverse drug reactions were reported: decreased appetite, abdominal pain, and diarrhoea. Each event does not occur in more than 2 patients Laboratory tests and vital signs are normal. There are no death or serious adverse events observed.	PEG+E is effective in treating constipation in children.
Hardikar, et al. [28]	78	PEG 3350	12 weeks`	1.4	7.1 (P<0.001)	1. Abdominal pain 2. pain on defaecation	1. 69% vs 4% (P<0.0001) 2. 79% vs 9% (P<0.0001)	 92% of the patients reported adverse events out of which 72% reported these events are unrelated to study medication. 6 SAEs and all are unrelated to study medication 4% of the patients were withdrawn due to poor compliance 	PEG 3350+electrolytes is a safe and effective treatment for constipation

Supplementary Table 2: Details of observational studies.

				Stool frequency/ week						
Author	No of patients	Duration of intervention	Intervention	Baseline	End of the treatment	P value	Other outcomes	Results	Safety data	End result
Pashankar, et al. [29]	83	>3 months	PEG 3350	Na	Na	Na	Na	Na	Diarrhoea, bloating, and flatulence are the most common adverse events reported which are minor. None of the patients stopped the medication All blood test results were normal, except for transient minimal alanine aminotransferase elevation unrelated to therapy in 9 patients	Long term peg therapy is safe and well accepted by children with chronic constipation with and without encopresis.
Pashankar, et al. [30]	24	8 weeks	PEG 3350	2.3	16.9	(P<0.001)	 1.stool consistency 2.weekly soiling events 3.painful defecation 4.fear of defecation 5.rectal faecal impaction 	1.3 vs 3.3 (P<0.0001) 10 vs 1.3 (P=0.003) 75% vs 0% (P<0.0001) 70% vs 5% (P<0.0001) 83% vs 22 (P=0.0006)	Diarrhoea, flatulence, and abdominal pain were reported in a few children but None of the patients stopped PEG treatment. All children reported willingness to take PEG therapy	Daily administration of PEG is an effective, safe, and palatable treatment for constipation
Pashankar, et al. [30]	74	>3 months	PEG 3350	2.9	9.9	(P<0.001)	1.stool consistency 2.Painful defecation 3.Blood in stools 4.Stool withholding 5.Rectal fecal impaction	1.4 to 3.1 (P<0.001) 81% to 5% (P <0.001 35% to 0% (P<0.001) 58% to 5 % (P<0.001) 40% to 5% (P<0.001)	No major clinical adverse effects related to PEG therapy.	Long-term PEG therapy is effective for the treatment of chronic constipation with and without encopresis in children
Dupont, et al. [31]	96 6-12 months 13 months to 3years 4 to 7 8 to 15 years	3 months	(PEG) 4000	3 2 2 2	11 7 8 9	(P<0.001) (P<0.001) (P<0.001) (P<0.001)	1.Hard stools 2.Fecal mass in the rectum	1. 87% to 0 (0%) (P<0.001) 2.90% to 4% (P<0.001) 3. 86% to 0% (P<0.001) 4. 83% to 13% (P<0.001) 1.33% to 0% 2. 47% to 4% 3. 54% to 0% 4. 52% to 5%	Almost 53% of the children had adverse effects related to PEG 4000 therapy. But there are no serious adverse effects.	In this dose determination study PEG 4000 is safe and effective in constipated children and children with fecal soiling with minimal adverse effects.