Lactulose versus Polyethylene Glycol for Chronic Constipation (Review)

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[Intervention Review]

Lactulose versus Polyethylene Glycol for Chronic Constipation

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ABSTRACT

Background

Constipation is a common clinical problem. Lactulose and Polyethylene Glycol (PEG) are both commonly used osmotic laxatives that have been shown to be effective and safe treatments for chronic constipation. However, there is no definitive data as to which provides the best treatment.

Objectives

To identify and review all relevant data in order to determine whether Lactulose or Polyethylene Glycol is more effective at treating chronic constipation and faecal impaction.

Search strategy

We searched the MEDLINE, EMBASE and CINAHL databases, and the Cochrane Central Register of Controlled Trials for all randomised controlled trials (RCTs) comparing the use of lactulose and polyethylene glycol in the management of faecal impaction and chronic constipation.

Selection criteria

Studies were included if they were randomised controlled trials which compared lactulose with polyethylene glycol in the management of chronic constipation.

Data collection and analysis

Data on study methods, participants, interventions used and outcomes measured was extracted from each study. Data was entered into the Cochrane Review Manager software (RevMan 5.0) and analysed using Cochrane MetaView.

Main results

In the present meta-analysis, we considered for the first time all ten randomised controlled trials so far performed. The findings of our work indicate that Polyethylene glycol is better than lactulose in outcomes of stool frequency per week, form of stool, relief of abdominal pain and the need for additional products. On subgroup analysis, this is seen in both adults and children, except for relief of abdominal pain.

Authors' conclusions

Polyethylene Glycol should be used in preference to Lactulose in the treatment of Chronic Constipation.

PLAIN LANGUAGE SUMMARY

Polyethylene Glycol should be used in preference to Lactulose in the treatment of Chronic Constipation.

Constipation is a common clinical problem, encompassing much more than reduced stool frequency. In this review we compared two commonly used osmotic laxatives, Lactulose and Polyethylene Glycol (PEG).

The findings of our work indicate that PEG is better than lactulose in outcomes of stool frequency per week, form of stool, relief of abdominal pain and the need for additional products. This is seen in both adults and children. Only exception is for relief of abdominal pain, where PEG is better than lactulose in children, but not in adults (no difference is seen).

We conclude that Polyethylene Glycol should be used in preference to Lactulose in the treatment of Chronic Constipation.

BACKGROUND

Description of the condition

Constipation is a common clinical problem, although published prevalence rates vary ranging from 2% to 35% in the published literature (Loening-Baucke 1993, Sondheimer 2002, Peppas 2008, Rao 2003, Lembo 2003, Johanson 1989, Talley 1993, Sandler 1987, Talley 2003,Higgins 2004, Frexinos 1998, Bassotti 2004), attributable to the lack of a single definition of constipation and study methodology. For many, this condition is chronic (Lembo 2003, Brandt 2005).

Patients often consider constipation to encompass much more than reduced stool frequency alone; a range of symptoms are described, such as hard or small stool, excessive straining, feelings of incomplete evacuation, abdominal discomfort or a requirement for digital manipulation to assist defecation (Sandler 1987, Arce 2002, Drossman 1997,Velio 1996). No widely accepted clinically useful definition of chronic constipation exists, but the Rome criteria - and most recently the Rome III (Longstreth 2006) - have been created by consensus to form a framework for establishing the diagnosis (Bassotti 2003) as the presence of 2 or more of the following symptoms for at least 3 months:

- Straining in at least 25% defecations
- Lumpy or hard stool in at least 25% defecations
- Sensation of incomplete evacuation in at least 25% defecations
- Sensation of anorectal obstruction / blockade in at least 25% defecations
- Manual manoeuvres to facilitate at least 25% defecations (e.g. digital evacuation, pelvic floor support)
- Fewer than 3 defecations per week
- Loose stools are rarely present without the use of laxatives
- Insufficient criteria for irritable bowel syndrome

Chronic constipation may also be associated with further suffering in the form of faecal impaction where a firm impassable mass of faeces forms in the colon or rectum, causing additional distressing symptoms of overflow diarrhoea and faecal soiling/incontinence, as well as having a negative impact on the overall quality of life and general well-being (Glia 1997, Irvine 2002, Thompson 1999, Damon 2004, Legoretta 2006, Talley 2004, Dennison 2005).

Causes of constipation can be divided in to primary (idiopathic) and secondary causes. Primary constipation is further classified in to normal-transit, slow-transit and dyssynergic constipation. Secondary causes include chronic laxative use and medications such as opioid analgesics, ferrous compounds and psychoactive drugs, as well as endocrine disorders (hypothyroidism, hyperparathyroidism, diabetes), neurological conditions (Hirschprung's disease, multiple sclerosis, Parkinson's disease, spinal cord injury), gastrointestinal conditions (Anal fissure, mucosal prolapse, colonic strictures or mass lesions with obstruction, idiopathic mega rectum) psychogenic conditions (anxiety, depression, eating disorders) and lifestyle factors (inadequate dietary fibre or fluid intake, extended bed rest and ignoring the urge to defecate). Despite this, the exact aetiology of chronic constipation remains largely unknown. It is postulated that patients may have reduced numbers of high-amplitude propagating contractions (Bassotti 2003).

In a bid to improve physical functioning and alleviate anxiety,

relief is often sought from the health care services, whose economic burden is substantial (Lembo 2003, Dennison 2005, Singh 2004). Treatment goals in chronic constipation aim to improve symptoms and restore bowel function by accelerating colonic transit and stimulating gut motility to ultimately facilitate defecation (Bleser 2005). Treatments include lifestyle changes, such as increased exercise, hydration and dietary fibre with the addition of simple laxatives. If these fail, the sufferers' quality of life may continue to decline as symptoms worsen, leading to general malaise, mood changes and depression (Legoretta 2006). This can trigger increased reliance on suppositories, laxatives, enemas and manual evacuation, the latter being a particularly traumatic procedure for children and humiliating for adults.

Description of the intervention

A wide range of pharmacological agents have been used in attempts to treat this difficult condition, but results are limited by the poor understanding of the pathophysiological mechanisms coupled with complex central and enteric interactions. The most recognised and acceptable treatment is the use of a group of drugs commonly referred to as 'laxatives' which are categorised in Table 1. Other classes of drugs used include prokinetics and antibiotics.

Table 1. Laxatives

Category	Example	Action	Benefit	Side Effects	Contra-Indications
Bulk-forming	Isphagula	Increase faecal mass to stimulate peristalsis	Useful treatment for small hard stools. Benefit Inflammatory Bowel Disease and Irritable Bowel Syndrome patients, and colostomy and Ileostomy patients	Abdominal distension, flatulence, GI obstruction or impaction	Difficulty swallowing, intestinal obstruction, colonic atony or faecal impaction.
Stimulant	Bisacodyl, Docusate, Senna	Increase intestinal motility	Patients unresponsive or intolerant of fibre	Abdominal cramp, Hypokalaemia	Intestinal obstruction
Softeners	Mineral oils, Arachis oil	Faecal softeners	Gentle action for haemorrhoids or anal fissure	Granulomatous reactions, lipoid pneumonia, interference with absorption of fat-soluble vitamins	Enemas can be painful and distressing for children
Osmotics	Lactulose, Polyethylene glycol (PEG), Magnesium hydroxide, Magnesium salts	Increase water content in large bowel. Lactulose is fermented by colonic bacteria which decrease gut pH, resulting in faecal volume expansion & accelerated transit.	Minimal electrolyte losses. PEG activity does not increase colonic gas	Lactulose: altered bowel flora causing bloating, flatulence, colic, excessive diarrhoea. PEG: abdominal distension and pain, nausea, excessive diarrhoea.	Lactulose: galactosaemia, intestinal obstruction. PEG: intestinal perforation or obstruction, paralytic ileus, severe inflammatory conditions of the GI tract (e.g. Crohn's, UC, toxic megacolon).

Lactulose and Polyethylene glycol (PEG) have been shown to be effective and safe treatments for chronic constipation (Candy 2006, Rendeli 2006,Dupont 2005, Brandt 2005, Voskuijl 2004, Bouhnik 2004, Gremse 2002, Christie 2002, Attar 1999, Freedman 1997, Fritz 2005, Mangin 2002, Guest 2004, Ferguson 1999), and are commonly used in both paediatric and adult populations. The alternative osmotic laxatives of magnesium hydroxide or magnesium salts are satisfactory for occasional use or where rapid bowel evacuation is required but tend not to be used in the long term, hence are not included in this study dealing with the management of chronic constipation (BNF 2007).

How the intervention might work

Lactulose and Polyethylene glycol (PEG) are osmotic laxatives widely used in the treatment of chronic constipation (Bouhnik 2004). These are non-absorbable, non-metabolised agents which increase the amount of water in the large bowel. Lactulose is a semi-synthetic disaccharide producing an osmotic diarrhoea of low faecal pH. PEG is an inert polymer which sequesters fluid in the bowel (BNF 2007).

Why it is important to do this review

Despite the wide variety of drugs aimed at treating constipation and faecal impaction, and the large sum of healthcare budget spent on these, evidence of their effectiveness is limited, with rates of successful treatment reported by specialist centres of only 50-60% (Sondheimer 2002, Schiller 2004).
Lactulose and Polyethylene glycol are both osmotic laxatives which are commonly used in the treatment of chronic constipation. However, there are no definitive data as to which provides the best treatment and economic outcome (Voskuijl 2004). Approximately ten randomised studies have been reported (Candy 2006, Rendeli 2006, Dupont 2005, Brandt 2005, Voskuijl 2004, Bouhnik 2004, Gremse 2002, Christie 2002, Attar 1999, Freedman 1997, Fritz 2005, Mangin 2002, Guest 2004, Ferguson 1999), providing enough information for a systematic review comparing these two agents for efficacy.

OBJECTIVES

To identify and review all relevant data in order to determine whether Lactulose or Polyethylene Glycol is more effective at treating chronic constipation and faecal impaction.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) comparing the use of lactulose and polyethylene glycol in the management of faecal impaction and chronic constipation. Both monotherapy and crossover studies were reviewed.

Types of participants

Patients diagnosed with chronic constipation (Rome III criteria) or faecal impaction, including both adults and children, treated with lactulose or polyethylene glycol.

Types of interventions

The specific comparison made was:
Treatment with lactulose versus polyethylene glycol in adults and children with chronic constipation and/or faecal impaction. Different treatment protocols were used.

Types of outcome measures

Primary outcomes

- Change in frequency of defecation

Secondary outcomes

- Use of additional products, e.g. alternative laxative agents, enemas
- Percentage in global improvement of symptoms
- Relief of abdominal pain

Search methods for identification of studies

We searched the MEDLINE, EMBASE and CINAHL databases, and the Cochrane Central Register of Controlled Trials (CENTRAL). There were no limitations based on language or date of publication. Bibilographies of all retrieved and relevant publications identified by these strategies were searched for further studies.
All searches were carried on January 2008.

Electronic searches

We searched the MEDLINE, EMBASE and CINAHL databases, and the Cochrane Central Register of Controlled Trials as above. For comprehensive search strategy see Appendix 1.

Searching other resources

In addition, we searched additional trials by scanning reference lists in relevant papers and conference proceedings and through correspondence with experts and pharmaceutical companies. The

customized search strategy for systematic reviews was used to identify relevant articles.

Data collection and analysis

Data from the selected studies was extracted using a paper data extraction form. Data was entered into the Cochrane Review Manager software (RevMan 5.0) and analysed using Cochrane MetaView.

Selection of studies

The reviewers (HLR, KT, JM) independently assessed titles and abstracts of the references identified by the search strategy according to the selection criteria. Full text copies of those articles and studies that appear to satisfy these criteria was obtained. When it was unclear from the title or abstract whether the paper fulfilled the criteria, or when there was disparity between reviewers, a full text copy was obtained. Obtained studies were individually assessed by two of the three reviewers (HLR, KT, JM) and then agreement obtained as to whether include or exclude a study. Any dispute was resolved by requesting a third independent review (HLR, KT, JM, RLN).

Studies were assessed for quality, with respect to methods of randomisation, allocation concealment, blinding of outcomes and drop-out rate.

Data extraction and management

Reviewers used a piloted data extraction sheet to summarise details of the studies. Data extraction was undertaken independently by the two reviewers and compared, with any dispute resolved by the third independent reviewer.

The following data was extracted from each study:

- Study methods
  - Definition and diagnostic criteria
- Participants
  - Number, source, age, gender, inclusion and exclusion criteria, duration of symptoms, previous treatments, underlying conditions
- Interventions
  - Run-in phase, treatment phase, follow-up
  - Or type, dose, duration, control used
- Outcomes
  - Change in frequency of defecation
  - Percentage global improvement, use of additional products, relief of abdominal pain

Assessment of risk of bias in included studies

The quality of the included trials was evaluated independently by the reviewers. It was assessed according to the four types of bias: Selection bias; Performance bias; Attrition bias and Detection bias.

Criteria for quality assessment included:

(1) Selection bias:

Allocation concealment:

A. Adequate: Use of randomisation method that did not allow investigator and participant to know or influence the allocation of treatment before eligible participants entered the studies.

B. Unclear: Randomization stated but no information on method used was available.

C. Inadequate: Use of alternate medical record numbers or unsealed envelopes as randomisation method, and/or there was information in the study indicating that investigators or participants could have influenced the allocation of treatment.

(2) Performance bias:

Blinding of care providers: Yes/No/Unclear

Blinding of participants: Yes/No/Unclear

Care providers and participants were considered not blinded if the intervention group could be identified in >20% of participants because of the side effects of treatment.

(3) Detection bias:

Blinding of outcome assessors: Yes/No/Unclear

(4) Attrition bias:

Intention-to-treat analysis:

A: Yes: All participants were analysed in the treatment group to which they were allocated, regardless of whether of not they received the allocated intervention.

B: No: Some participants (<5%, 5-10%, 10-20 %,> 20%) were not analysed in the treatment group to which they were randomised because they did not receive study intervention; they withdrew from the study, or because of protocol violation.

C: Unclear: Inability to determine if patients were analysed according to the intention-to-treat principle after contract with the authors.

Completeness of follow-up: Completeness follow-up of at last 85% was considered to be adequate.

Clarification from the author was sought if the published data provided inadequate information for the review. Discrepancies were resolved by consensus. From the quality assessment of the trails the potential risk of bias was summarized into three categories as described in the Cochrane handbook.

Clarification from the author was sought if the published data provided inadequate information for the review. Discrepancies were resolved by consensus. From the quality assessment of the trails the potential risk of bias was summarized into three categories as described in the Cochrane handbook.

Risk of bias interpretation relationships to individual criteria

A:Low risk of bias: plausible bias unlikely to all of the criteria met seriously alter the results.

B: Moderate risk of bias: plausible bias that raises one or more criteria partly met some doubt about the results.

C:High risk of bias: plausible bias that seriously two or more criteria not met weakens confidence in the results.

Measures of treatment effect

The primary outcome of frequency of defecation were assessed using weighted mean difference with 95% confidence intervals. The secondary outcomes were dichotomous data and were assessed by calculating the relative risks or risk ratios (RR) with 95% confidence intervals. RR less than 1.0 favoured the intervention group, indicating that PEG was superior when compared to Lactulose in the treatment of chronic constipation.

Unit of analysis issues

The primary outcome - frequency of defecation - was a continuous outcome (measured as the number of defecations per week). The analysis used the weighted mean difference + 95% confidence intervals. The secondary outcome of "use of associated products" was dichotomous (yes or no) and "assessment of improvement in abdominal pain" was analysed as a score, or dichotomised.

Dealing with missing data

The authors of included studies were contacted to supply missing data. Missing data and drop-outs/attrition was assessed for each included study, and the extent to which the result/conclusion of the review could have been altered by the missing data was assessed and discussed. When data were missing from the paper, an attempt was made to contact the authors to obtain the missing information. When significant gaps in data occurred and we were unable to obtain the missing data, we excluded these studies from review.

Assessment of heterogeneity

Clinical heterogeneity was assessed by comparing the distribution of important participant factors (age, sex) between trials and trial factors (randomisation concealment, blinding of outcome assessment, and losses to follow-up, treatment regimens).Statistical heterogeneity was assessed by examining I^2 (Higgins 2008) or Chi-Squared test. If significant heterogeneity was present (i.e.I^2>= 50%) (Higgins 2008), trials were explored to investigate for possible explanations. In the case of the absence of heterogeneity, data was analysed using fixed effects model.

Assessment of reporting biases

Where possible, we performed funnel plots to assess the chance of report bias and presented these using a table of bias.

Data synthesis

The analyses were performed in RevMan version 5.0. Results were shown using the approach recommended in the Cochrane Handbook (Higgins 2008). Dichotomous data were presented as relative risks (RR) with 95% confidence intervals. All randomised patients included were analysed using the intention-to-treat principle. We assessed heterogeneity between the trails using I^2. Where the interventions were the same or similar enough, we synthesized results in meta-analysis if there was no important clinical heterogeneity. In the case of the absence of heterogeneity, data were analysed using fixed-effects model. Random-effects models were used if there was heterogeneity. We performed subgroup analyses to assess the impact of these possible sources of heterogeneity, where appropriate. The authors of included studies were contacted to supply missing data. Funnel plots were drawn if sufficient studies were found.

Subgroup analysis and investigation of heterogeneity

If data permitted, we conducted subgroup analyses for studies using children compared with adults, and also endpoints if there were many different endpoints used between studies. As trials were conducted by different groups of investigators at different periods of time, some were heterogeneous. We explored heterogeneity between trial results using multi-step process including: (1) Forest plots were examined and the presence or absence of overlap in the confidence intervals noted. Lack of overlap of confidence intervals indicated heterogeneity. (2): We looked at the I^2 statistic to describe the proportion of the variability in the results that was due to heterogeneity (Higgins 2008). (3):Chi-Squared test for heterogeneity was performed and data considered heterogenous if $p<0.1$. (4) If significant heterogeneity was detected, possible explanations were sought.

Sensitivity analysis

If a sufficient number of randomised trials were identified, we performed sensitivity analysis to explore the impact of study quality. Studies with clearly inadequate allocation of concealment were excluded. A second sensitivity analysis would be based on excluding outlying results.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

See Characteristics of included studies and Characteristics of excluded studies

Results of the search

We assessed 103 references from the primary search and additional search methods described, until 24/01/2008. From their abstracts, 16 of these potentially meet our inclusion criteria and the full papers were obtained. Following this review, we excluded 6 of these

trials (see Characteristics of excluded studies). A total of ten trials were included in the review.

The ten trials enrolled a total of 868 participants (range 37 - 191), of which 322 were adults and 546 were children. All trials were reported in English, except for Zhang 2003, Wang 2007. The trials included in the review were published between 1997 and 2007.

Location:

The trials were conducted in six different countries. The trials were conducted in a variety of different settings, including hospital inpatients, outpatients, local community.

Funding:

Six trials did not state their source of funding. One trial stated it had no funding. Three trials reported a pharmaceutical company provided funding Dupont 2005, Bouhnik 2004, Candy 2006

Patient Symptoms:

Trials used different inclusion criteria for the participants. Four studies used the Rome Diagnostic Criteria. The remaining six studies used a range of definitions of chronic constipation.

Participant Age:

Patricipant age ranged from 3 months to 70 years. Adults only were recruited for 4 studies.

Included studies

From 1997 to 2007, 10 randomised controlled trials were conducted that compared lactulose with polyethylene glycol (+/- placebo) for the treatment of chronic constipation.

Excluded studies

Four studies were excluded because they were not randomised controlled trials (Brandt 2005, Christie 2002, Fritz 2005, Guest 2004), one was an abstract with no data available to be obtained from the authors at this time (Ferguson 1999), and one only included patients with acute constipation (Van der Spoel 2007).

Risk of bias in included studies

See Figure 1, Figure 2.

Figure 1. Methodological quality graph: review authors' judgments about each methodological quality item presented as percentages across all included studies.

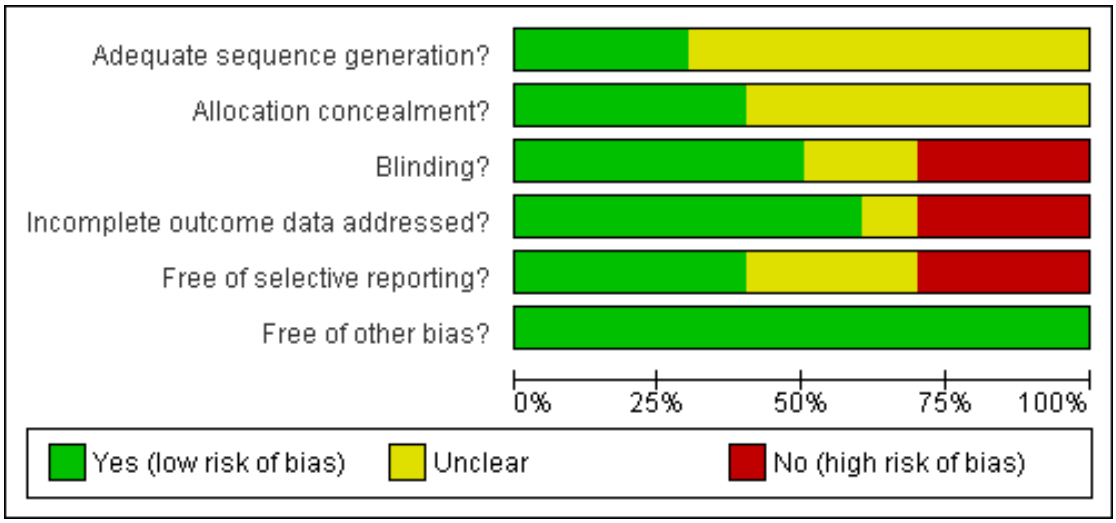
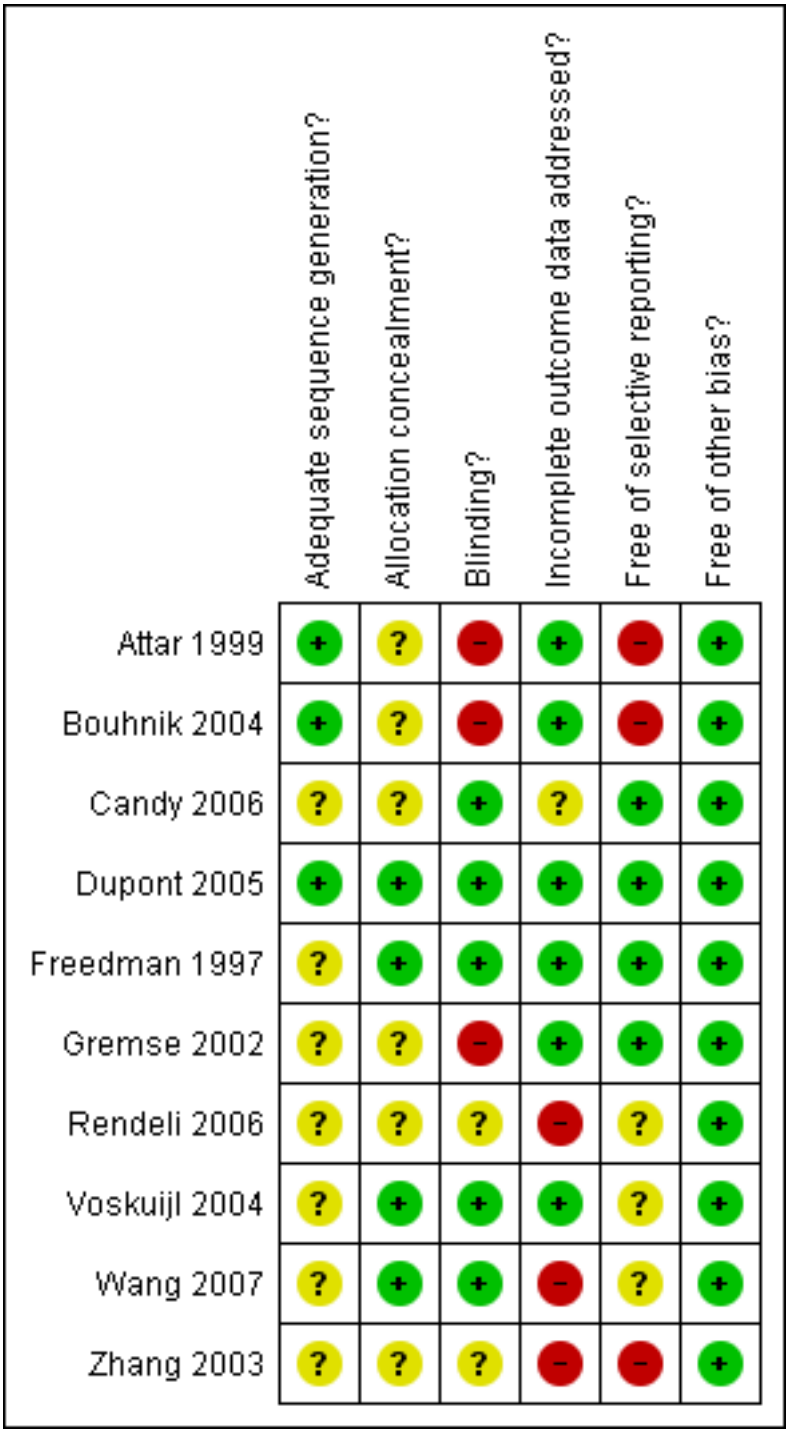


Figure 2. Methodological quality summary: review authors' judgments about each methodological quality item for each included study.



Allocation

Three of the ten included trials reported adequate generation of the allocation sequence. Attar 1999 and Dupont 2005 used a randomised list. Freedman 1997 employed a Latin square design.

Blinding

Five trials Candy 2006, Dupont 2005, Freedman 1997, Voskuijl 2004, Wang 2007 reported to be double-blind studies with blinding of the participants, care providers and outcome assessors. Two trials Attar 1999, Bouhnik 2004 reported single-blinding with blinding of the assessors but not the participants or care providers. One trial Gremse 2002 reported that the study was undertaken unblinded with a cross-over design. Two trials Rendeli 2006, Zhang 2003 were unclear regarding blinding.

Incomplete outcome data

The following studies reported the outcomes below, however due to the use of incomparable scales or incomplete raw data, they could not be included in the meta-analysis.

Stool frequency per week:

Dupont 2005 reported his data using medians and Interquartile ranges which we were unable to analyse in this meta analysis.

Freedman 1997 reported form of stool motions per week as hard, soft or loose.

There was incomplete data for analysis by Rendeli 2006, data was only reported in Chart form with no raw data.

There was incomplete data for analysis by Wang 2007.

Form of stool (Bristol Stool Score):

There was incomplete data for analysis by Candy 2006, only giving a p value which we were unable to analyse in this meta analysis

Freedman 1997, Gremse 2002 and Dupont 2005 reported form of stool using their own qualitative scale, not the Bristol Stool Score.

Relief of abdominal pain:

Attar 1999 reported his data using his own scale of 1-3 using the median, which we were unable to analyse in this meta analysis.

There was incomplete data for analysis by Freedman 1997 and Candy 2006, only giving a p value which we were unable to analyse in this meta analysis.

Did not use additional products:

There was incomplete data for analysis by Freedman 1997.

Selective reporting

Our primary outcome of stool frequency per week was reported by all authors except for Zhang 2003.Unusually, they reported the time to pass stool.

Other potential sources of bias

None identified.

Effects of interventions

All trials compared the used of lactulose and Polyethylene glycol using a combination of outcomes to assess this.

Stool Frequency per week:

Five trials Attar 1999, Bouhnik 2004, Candy 2006, Gremse 2002, Voskuijl 2004 reported stool frequency per week. Singularly taken, all showed that PEG resulted in a higher stool frequency per week when compared with Lactulose Analysis 1.1.

Data for Attar 1999: There were 60 patients in the Polyethylene glycol group, with a mean stool frequency of 1.3 per week (S.D. 0.7) compared with 55 patients in the Lactulose group, with a mean stool frequency of 0.9 per week (S.D. 0.6).

Data for Bouhnik 2004: There were 32 patients in the Polyethylene glycol group, with a mean stool frequency of 1.26 per week (S.D. 0.65) compared with 33 patients in the Lactulose group, with a mean stool frequency of 1.12 per week (S.D. 0.33).

Data for Candy 2006: There were 27 patients in the Polyethylene glycol group, with a mean stool frequency of 9.4 per week (S.D. 4.56) compared with 26 patients in the Lactulose group, with a mean stool frequency of 5.9 per week (S.D. 4.29).

Data for Gremse 2002: There were 37 patients in the Polyethylene glycol group, with a mean stool frequency of 14.8 per week (S.D. 1.4) compared with 37 patients in the Lactulose group, with a mean stool frequency of 13.5 per week (S.D. 1.5).

Data for Voskuijl 2004: There were 50 patients in the Polyethylene glycol group, with a mean stool frequency of 7.12 per week (S.D. 5.14) compared with 50 patients in the Lactulose group, with a mean stool frequency of 6.43 per week (S.D. 5.18).

We found there to be significant heterogeneity with this outcome (Heterogeneity: $Chi^2 = 17.58$, df = 4 (P = 0.001); $I^2 = 77\%$). On removing both Candy 2006 and Gremse 2002 from the analysis this greatly reduces (Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 10.88$, df = 3 (P = 0.01); $I^2 = 72\%$ on removing Candy 2006 alone. Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 9.30$, df = 3 (P = 0.03); $I^2 = 68\%$ on removing Gremse 2002 alone. Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.32$, df = 2 (P = 0.31); $I^2 = 14\%$ on removing both studies from the analysis). When looking at these studies we found that one possible source could be that in the Candy 2006 study, the participants had already undergone a prior phase of the study where participants had been successfully disimpacted prior to the comparative stage of the trial. Both studies, especially Gremse 2002, had a small number of participants (Candy 2006: 58 participants, Gremse 2002: 37 participants). The only other interesting point is that both of these studies were the only crossover trials analysed in this outcome. No other source of heterogeneity could be found.

Form of Stool (Bristol Stool Score):
Two trials Wang 2007, Zhang 2003 reported form of stool on the Bristol Stool Scale. Singularly taken, both studies reported a higher Bristol Stool Score when using PEG compared with lactulose (softer stool) Analysis 2.1.
Data for Wang 2007: There were 105 patients in the Polyethylene glycol group, with a mean Bristol stool score of 4.26 (S.D. 0.89), compared with 111 patients in the Lactulose group, with a mean Bristol stool score of 3.63 (S.D. 1.33).
Data for Zhang 2003: There were 41 patients in the Polyethylene glycol group, with a mean Bristol stool score of 4.0 (S.D. 0.3), compared with 44 patients in the Lactulose group, with a mean Bristol stool score of 2.9 (S.D. 0.2).
We found there to be significant heterogeneity with this outcome (Heterogeneity: $Chi^2 = 8.31$, df = 1 (P = 0.004); $I^2 = 88\%$). However, owing to there only being two studies comparable we were unable to remove either study to investigate which was the possible source of this. Differences between the studies include the following: Wang 2007 had over twice the number of patients compared with Zhang 2003 (191 compared with 81) and Wang 2007 was a paediatric study whereas Zhang 2003 was an adult study. Wang 2007 was also double-blinded compared with Zhang 2003.

Relief of Abdominal Pain:
Three trials Bouhnik 2004, Dupont 2005, Wang 2007 reported relief of abdominal pain. Singularly taken, two trials favour PEG in this outcome; Dupont 2005 and Wang 2007. Bouhnik 2004 found Lactulose and PEG to be comparable in this outcome. This study included only 65 patients, the other two studies included 235 patients Analysis 3.1. (PEG lac - events total)

26	33	26	32
9	11	3	8
79	105	63	111

Data for Bouhnik 2004: There were 33 patients in the Polyethylene glycol group, and 26 of these had relief of abdominal pain with treatment (79%). This compares to the 32 patients in the Lactulose group, 26 of which had relief of abdominal pain following treatment (81%).
Data for Dupont 2005: There were 11 patients in the Polyethylene glycol group, and 9 of these had relief of abdominal pain with treatment (82%). This compares to the 8 patients in the Lactulose group, 3 of which had relief of abdominal pain following treatment (38%).
Data for Wang 2007: There were 105 patients in the Polyethylene glycol group, and 79 of these had relief of abdominal pain with treatment (75%). This compares to the 111 patients in the Lactulose group, 63 of which had relief of abdominal pain following treatment (57%).
The result of this outcome was not heterogenous (Heterogeneity: $Chi^2 = 3.60$, df = 2 (P = 0.17); $I^2 = 44\%$).

Did not Require Additional Products:
Three trials Attar 1999, Candy 2006, Dupont 2005 reported on use of additional products. Singularly taken, all favoured PEG as requiring less use of additional products Analysis 4.1.
Data for Attar 1999: There were 50 patients in the Polyethylene glycol group, and 42 of these did not require additional products alongside treatment (84%). This compares to the 49 patients in the Lactulose group, 32 of which did not require additional products (65%).
Data for Candy 2006: There were 27 patients in the Polyethylene glycol group, and 27 of these did not require additional products alongside treatment (100%). This compares to the 25 patients in the Lactulose group, 17 of which did not require additional products (68%).
Data for Dupont 2005: There were 32 patients in the Polyethylene glycol group, and 27 of these did not require additional products alongside treatment (84%). This compares to the 42 patients in the Lactulose group, 25 of which did not require additional products (60%).
The result of this outcome was not heterogenous (Heterogeneity: $Chi^2 = 2.20$, df = 2 (P = 0.33); $I^2 = 9\%$).

DISCUSSION

Lactulose and Polyethylene glycol are both osmotic laxatives which are commonly used in the treatment of chronic constipation. However, there are no definitive data as to which provides the best treatment and economic outcome (Voskuijl 2004). Approximately ten randomised studies have been reported (Candy 2006, Rendeli 2006, Dupont 2005, Brandt 2005, Fritz 2005, Voskuijl 2004, Bouhnik 2004, Guest 2004, Gremse 2002, Christie 2002, Mangin 2002, Attar 1999, Ferguson 1999, Freedman 1997), providing enough information for a systematic review comparing these two agents for efficacy.

Summary of main results

In the present meta-analysis, we considered for the first time all ten randomised controlled trials so far performed. The findings of our work indicate that Polyethylene glycol is better than lactulose in outcomes of stool frequency per week, form of stool, relief of abdominal pain and the need for additional products. On subgroup analysis, this is seen in both adults and children, except for relief of abdominal pain. The single paper by Bouhnik 2004 favours Lactulose over PEG on this outcome alone, but subgroup analysis on this outcome is limited by only a single paper reporting this outcome for adults.

Overall completeness and applicability of evidence

In the light of the improved efficacy of Polyethylene glycol, the findings of the present meta-analysis must be taken into consideration in the therapeutic management of patients with chronic constipation.

Quality of the evidence

Overall, we feel there is sufficient evidence, looking at all the outcomes across all of the randomised controlled trials, that Polyethylene Glycol is superior to Lactulose in the management of chronic constipation.

When analysing the outcome of stool frequency we found significant heterogeneity and all studies were reviewed for potential sources. We assessed each study individually for quality.

Attar 1999 appeared to be a well-designed and carried-out study. They gave an adequate definition of chronic constipation. The generation of their allocation sequence was adequate and the study was performed blind. They performed a priory calculation of sample size and their population sample was 115, with both groups comparable at baseline. The treatment phase was well explained and seemed adequate for both groups. A good comparison was made between the two products with assessed outcomes including stool frequency, relief of abdominal pain, use of additional products, ease of passage, adverse events.

Bouhnik 2004 appeared to be a well-designed and carried-out study. They gave an adequate definition of chronic constipation. The generation of their allocation sequence seemed adequate, however the study was not blinded to the participants or the physicians. They performed a priory calculation of sample size and their population sample was 65, with both groups comparable at baseline. The treatment phase was well explained and seemed adequate for both groups. A good comparison was made between the two products with assessed outcomes including stool frequency, relief of abdominal pain, ease of passage, adverse events.

Candy 2006 appeared to be a well-designed and carried-out study on the whole but it is important to note that this was a two-stage trial with the second phase only being relevant to our analysis, hence providing a possible source of heterogeneity. A definition of chronic constipation was given in this study, however it was felt to be inadequate, with no mention of Rome criteria. The generation of their allocation sequence was felt to be inadequate, however the study was performed blind. They performed a priory calculation of sample size and their population sample was 65, with both groups comparable at baseline. The treatment phase was explained although in comparison with some other studies, no adjustment of dosage was made depending on tolerance and symptoms as this was a two phase trial with the comparison between the two interventions being made after disimpaction, more as a maintenance therapy. This paper differed significantly from the rest in this respect. Outcomes assessed included only stool frequency and use of additional products.

Dupont 2005 appeared to be a well-designed and carried-out study. They gave an adequate definition of chronic constipation. The generation of their allocation sequence was adequate and the study was performed blind. They performed a priory calculation of sample size and their population sample was 101, with both groups comparable at baseline. The treatment phase was well explained and seemed adequate for both groups. A good comparison was made between the two products with assessed outcomes including stool frequency, form of stool, relief of abdominal pain, use of additional products.

Gremse 2002 appeared to be a well-designed study although there was a lot of missing data and so it is difficult to comment with much certainty. A definition of chronic constipation was not given. The generation of their allocation sequence was not states and the study was performed unblinded. It was not stated whether they performed a priory calculation of sample size and their population sample was small at 44, however this was a cross-over design. The treatment phase was explained although in comparison with some other studies, no adjustment of dosage was made depending on tolerance and symptoms. A good comparison was made between the two products with assessed outcomes including stool frequency, form of stool, ease of passage, transit time.

Freedman 1997 appeared to be a well-designed study although there was a lot of missing data and so it is difficult to comment with much certainty. A definition of chronic constipation was given in this study, however it was felt to be inadequate with no quantifiable statement. The generation of their allocation sequence was adequate and the study was performed blind. No priory calculation of sample size was performed, however their population sample was 57 with a cross-over design. The treatment phase was not explained. A good comparison was made between the two products with assessed outcomes including stool frequency, form of stool, relief of abdominal pain and use of additional products, however none of these were analysed in the meta analysis due to incomparable scales used.

Rendeli 2006 appeared to be an adequately designed and carried-out study. They gave an adequate definition of chronic constipation. The generation of their allocation sequence was not

stated and the study was performed unblinded. They did not state whether they performed a priory calculation of sample size. Their population sample was 80, with both groups comparable at baseline. The treatment phase was well explained and seemed adequate for both groups. The comparison between the two products with assessed using only stool frequency.

Voskuijl 2004 appeared to be a well-designed and carried-out study. They gave an adequate definition of chronic constipation. The generation of their allocation sequence was not stated. The study was performed blind. They performed a priory calculation of sample size and their population sample was 100, with both groups comparable at baseline. The treatment phase was well explained and seemed adequate for both groups. The comparison between the two products with assessed using only stool frequency.

Wang 2007 appeared to be a well-designed and carried-out study. No adequate definition of chronic constipation was given. The generation of their allocation sequence was not stated. The study was performed blind. They did not state whether they performed a priory calculation of sample size and their population sample was 227. It was unclear whether groups were comparable at baseline. The treatment phase was well explained and seemed adequate for both groups. A good comparison was made between the two products with assessed outcomes including stool frequency, form of stool, relief of abdominal pain, adverse events.

Zhang 2003 appeared to be the least well designed and carried-out study of those used in the meta analysis although it is important to mention that the review was translated from Mandarin and some information may have been lost at this point. They gave an adequate definition of chronic constipation. The generation of their allocation sequence was not stated. It was unclear whether the study was performed blind. They did not state whether they performed a priory calculation of sample size and their population sample was 85, with both groups comparable at baseline. The treatment phase was well explained and seemed adequate for both groups. The comparison between the two products with assessed using only form of stool and adverse events.

As mentioned previously, on removal of the Candy 2006 and Gremse 2002 studies, heterogeneity in this outcome improved. The possible causes we found for this was a small number of participants in both trials, crossover design and the previous disimpaction of patients in the Candy 2006 study. No other source of heterogeneity could be found.

Potential biases in the review process

Some included trials were drug company sponsored studies. Bouhnik 2004 sponsored by Solvay Pharma who supplied the PEG 4000 used in the study, however Solvay Duphar B.V. supplied the Lactulose. Norgine Pharmaceuticals sponsored Candy 2006, it was not declared whether they supplied or produce either drug. Dupont 2005 were supported by Ipsen who packaged both Lactulose and PEG used in this trial.

Agreements and disagreements with other studies or reviews

The American College of Gastroenterology 2005 recommended that both PEG and lac are effective at improving stool frequency and stool consistency in patient with chronic constipation. However they only found two randomised controlled trials comparing these and did not provide reference or describe their search strategy. This paper is expert opinion considering the evidence available.

Ramkumar 2005 used Attar 1999 and Freedman 1997 to conclude that lactulose is less efficacious and has more side effects than PEG. They quote Christie 2002, suggesting that PEG is more cost-effective than Lactulose for treating chronic constipation, particularly in the National Health Service.

AUTHORS' CONCLUSIONS

Implications for practice

Polyethylene Glycol should be used in preference to Lactulose in the treatment of Chronic Constipation.

Implications for research

A standardised validated scale should be used for form of stool - e.g. Bristol Stool Score.

A standard definition of chronic constipation to be used - e.g. Rome II criteria.

Further information on subgroups, such as the elderly population would provide greater strength to this evidence.

Studies involving a chronic condition should consider long-term outcomes and therefore a cross-over design may not be the most appropriate way to look at these conditions.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Attar 1999

Methods	Generation of allocation sequence: a randomised list was established by the statistician. Allocation concealment: was not described. Blinding: As the two treatments differed in appearance and taste, the study was not conducted double blind. Investigators were unaware of the allocation of treatments. Inclusion of all randomised patients: All randomised patients were included in data analysis.
Participants	Number: 115 Age: 55 +/- 23 years (mean +/- S.D.) Source: Ten centres in France and Scotland. Patients were recruited from both general and geriatric hospitals, mainly from outpatient departments. Inclusion criteria: At least 18 years of age. The diagnosis of chronic idiopathic constipation was based on presence for at least three months of less than three stools per week and/or straining at stool. Patients older than 45 years required exclusion of constipation secondary to colonic disease, verified by colonoscopy or barium enema performed within the last 5 years. Exclusion criteria: Patients taking concomitant medications which could modify bowel habit and those suffering from severe liver, renal or cardiac diseases. Pregnant and breast-feeding women.
Interventions	10g Lactulose diluted in 15mls water or 13.12g PEG 3350, 0.18g sodium bicarbonate, 0.35g sodium chloride, 0.05g potassium chloride, 0.01g acesulfame-K and J2076 lemon flavours. Patients were instructed to take two sachets per day of the medications, in two divided doses, each sachet being diluted in 125mls water. If stools became liquid, participants could reduce the dosage. After two weeks patients were given the option to change the dosage based on efficacy and tolerance. No other treatments for constipation were allowed in this study, except for suppositories and micro-enemas.
Outcomes	Included in review: Number of stools per week, Use of additional products Excluded from review: Straining at stool, Liquid stools, Abdominal pain, Bloating/flatus/rumbling. All of these used a non-comparable symptom score scale.
Notes	Location: Scotland and France Source of funding: Not stated Attempts to clarify information: not required Language of Publication: English

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	A randomised list was established by the statistician. Inclusion of all randomised patients: All

Attar 1999 (*Continued*)

		randomised patients were included in data analysis.
Allocation concealment?	Unclear	Allocation concealment was not described.
Blinding? All outcomes	No	As the two treatments differed in appearance and taste, the study was not conducted double blind. Investigators were unaware of the allocation of treatments.
Incomplete outcome data addressed? All outcomes	Yes	All randomised patients were included in data analysis.
Free of selective reporting?	No	Did not report data on Form of stool
Free of other bias?	Yes	

Bouhnik 2004

Methods	Generation of allocation sequence: Sealed envelopes containing individual randomisation Allocation concealment: Unclear. Blinding: As the two treatments varied in appearance and taste, the study was blind only to the bacteriologists and biochemists, but not for the physicians and patients. Inclusion of all randomised: All analyses were performed as intention to treat procedures.
Participants	Number: 65 Age of patients: 57 +/- 18 years (mean +/- S.D.) Source: Patients in primary care. Inclusion criteria: Chronic idiopathic constipation diagnosed based on Rome I diagnostic criteria. An organic cause of constipation was excluded by the General Practitioner. Exclusion criteria: Patients taking concomitant medications which may modify bowel habit, severe liver disease, renal or cardiac diseases and pregnant or breast-feeding women.
Interventions	Patients were treated with either PEG 4000 electrolyte solution or lactulose for four weeks. In the first week 2 sachets of medication were taken per day. In the second week patients were given an option to change the dosage depending on efficacy and tolerance. For the third and fourth weeks the investigator changed the treatment dose based on the results of the second week.
Outcomes	Included in review: Stool frequency. Relief of abdominal pain. Excluded from review: Difficulty in defecation, straining on passage, borborygmi, bloating, fresh stool analysis, frozen stool analysis.
Notes	Location: Paris, Lille and Nantes, France Date: March-December 1998 Source of funding: Solvay Pharma, 42 rue Rouget de Lisle, F-92151, Suresnes Cedex, France Attempts to clarify information: not required.

Bouhnik 2004 (*Continued*)

	Language of Publication: English

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Sealed envelopes containing individual randomisation
Allocation concealment?	Unclear	Unclear
Blinding? All outcomes	No	As the two treatments varied in appearance and taste, the study was blind only to the bacteriologists and biochemists, but not for the physicians and patients.
Incomplete outcome data addressed? All outcomes	Yes	All analyses were performed as intention to treat procedures.
Free of selective reporting?	No	Did not report data on Form of Stool or use of additional products
Free of other bias?	Yes	

Candy 2006

Methods	Generation of allocation sequence: Not described. Allocation concealment: was not described. Blinding: Children and investigators were blinded as to the medication dispensed. Inclusion of all randomised: Data was summarised by randomised treatment group for the intent-to-treat and per protocol overall populations
Participants	Number: 58 Age: 2-11 years Source: Children who were successfully disimpacted during Phase I of the study (oral PEG+E as inpatient). Inclusion criteria: Intractable constipation that had failed to respond to conventional treatment. Exclusion criteria: Conditions contra-indicating the use of PEG-E or lactulose, including intestinal perforation or obstruction, allergy, paralytic ileus, toxic megacolon, Hirschsprung disease, severe inflammatory bowel disease, uncontrolled renal/hepatic/cardiac disease, uncontrolled endocrine disorder or any neuromuscular disorder affecting bowel function.
Interventions	The children received oral maintenance doses of PEG-E or lactulose commencing with one half of the number of sachets required for disimpaction in Phase I, for twelve weeks.

Candy 2006 (*Continued*)

Outcomes	Included in review: Stool frequency. Use of additional products. Excluded from review: Predominant bowel movement form, pain, straining, rectal bleeding, abdominal pain, soiling, overall rating of treatment. All of these outcomes used non-comparable scales. Adverse effects were also discussed,
Notes	Location: Paediatric Gastroenterology Service, Royal West Sussex NHS Trust, Chichester, UK Source of funding: Norgine Pharmaceuticals Ltd, Harefield, Middlesex, UK Attempts to clarify information: not required Language of Publication: English

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not described.
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	Children and investigators were blinded as to the medication dispensed.
Incomplete outcome data addressed? All outcomes	Unclear	Data was summarised by randomised treatment group for the intent-to-treat and per protocol overall populations
Free of selective reporting?	Yes	Reported data on all outcomes however, for form of stool and relief of abdominal pain he only gave p values.
Free of other bias?	Yes	

Dupont 2005

Methods	Generation of allocation sequence: randomisation list Allocation concealment: double-dummy design with patients receiving paired sachets Blinding: double-blind Inclusion of all randomised: 98 patients were randomised but 2 dropped out before study drug intake: one withdrew their consent and one was found not to meet the inclusion criteria. Efficacy and tolerance were assessed on an intention to treat basis.
Participants	Number: 96 Source: 3 hospital centres in France Inclusion criteria: Ambulatory children aged 6 months to 3 years with constipation despite dietary treatment for at least one month. Constipation defined as less than one stool per day for more than one month in children aged 6 to 12 months and less than 3 stools per week for more than 3 months in children aged 13 months to 3 years.

Dupont 2005 (*Continued*)

	Exclusion criteria: History of intractable faecoma or organic gastrointestinal disease, neurological, endocrine or metabolic disorders, allergic disease or allergies.
Interventions	Patients received either one 3.33g sachet of lactulose and one 4g sachet of placebo or one 4g sachet of PEG4000 and one 3.33g sachet of placebo at breakfast. In children aged 13 months to 3 years the dose could be doubled if ineffective. If this dose was unsuccessful, one glycerol enema could be used for a maximum of three consecutive days. If liquid stools were produced for more than one day or more than two or three stools per day the dose could be reduced by one pair of sachets per day.
Outcomes	Included in review: Relief of abdominal pain, Use of additional products Excluded from review: Stool frequency, Form of stools. Non-comparable scales were used. Adverse effects were also discussed.
Notes	Location: France Date: From July 2000 Source of funding: Ipsen, Paris, France Attempts to clarify information:not required Language of Publication: English

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Randomisation list
Allocation concealment?	Yes	Double-dummy design with patients receiving paired sachets
Blinding? All outcomes	Yes	Double-blind
Incomplete outcome data addressed? All outcomes	Yes	Efficacy and tolerance were assessed on an intention to treat basis.
Free of selective reporting?	Yes	All outcomes were reported.
Free of other bias?	Yes	

Freedman 1997

Methods	Generation of allocation sequence: not described Allocation concealment: prospective, randomised, double-blind, cross-over design utilising latin-square assignment. Blinding: double blind Inclusion of all randomised: 57 patients were recruited and 57 completed the protocol.

Freedman 1997 (*Continued*)

Participants	Number: 57 Source: the Sinai Hospital Drug Dependency Program. Inclusion criteria: Drug-dependent men and women involved in a methadone maintenance programme, who complained of constipation and had previously sought the use of laxatives, aged 18-50 years. Exclusion criteria: Women were required to be neither pregnant nor lactating. A history of colonic surgery, childhood constipation requiring more than one bowel-purging procedure per month, adult onset constipation predating methadone use, haem-positive stool of unknown aetiology, those deemed unreliable for a seven week follow-up period, and those who had a history of rectal bleeding within the last month.
Interventions	After one week control period during which patients received no treatment, a latin square assignment was used to evaluate three regimens in random order. Treatments included 240mls of identically flavoured 1) placebo (water), 2) lactulose (30mls diluted in water to 240mls), 3) Go-Lytely Lax (polyethylene glycol/electrolyte solution).
Outcomes	Included in review: None Excluded from review: Number of hard stools, number of soft stools and number of loose stools per week. Frequency of excessive gas per week, frequency of severe abdominal cramping. Additional product requirements were also discussed.
Notes	Location: Sinai Hospital, Baltimore, Maryland, USA. Source of funding: None stated Attempts to clarify information: attempted to contact authors via e-mail to obtain raw data for outcomes with incomparable scales/no data. Language of Publication: English

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not described
Allocation concealment?	Yes	Cross-over design utilising latin-square assignment.
Blinding? All outcomes	Yes	Double-blind
Incomplete outcome data addressed? All outcomes	Yes	All randomised patients completed the study and were included in the analysis
Free of selective reporting?	Yes	All outcomes were reported.
Free of other bias?	Yes	

Gremse 2002

Methods	Generation of allocation sequence: not stated Allocation concealment: not applicable as unblinded Blinding: Unblinded, randomised, cross-over design Inclusion of all randomised: 44 patients were enrolled in the study, 7 patients withdrew in the first two weeks due to lack of efficacy. These 7 were not included in analysis.
Participants	Number: 37 Source: patients referred for subspeciality evaluation of constipation Inclusion criteria: Aged 2 to 16 years, suffering from constipation. Exclusion criteria: Patients with organic disease of the large or small bowel, known allergy to PEG or lactulose, previous GI surgery, renal or heart failure, bowel obstruction, ileus, pregnancy, lactation, galactosaemia, or diabetes mellitus.
Interventions	Patients received either PEG 3350 (10g/m^2/day) or lactulose (1.3g/kg/day) orally for two weeks, followed by the other agent for two weeks.
Outcomes	Included in review: stool frequency per week, Excluded from review: total and segmental colonic transit time, global assessment by parent, score for stool form, ease of passage.
Notes	Location: Division of Pediatric Gastroenterology and Nutrition, University of South Alabama, USA Source of funding: not stated Attempts to clarify information: not required Language of Publication: English

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not stated
Allocation concealment?	Unclear	Not applicable as unblinded
Blinding? All outcomes	No	Unblinded
Incomplete outcome data addressed? All outcomes	Yes	44 patients were enrolled in the study, 7 patients withdrew in the first two weeks due to lack of efficacy. These 7 were not included in analysis.
Free of selective reporting?	Yes	Did not report on relief of abdominal pain or use of additional products
Free of other bias?	Yes	

Rendeli 2006

Methods	Generation of allocation sequence: This is a randomised controlled clinical trial with parallel group design. Allocation concealment: Not stated Blinding: Not stated Inclusion of all randomised: 70 patients were randomised, 2 patients did not enter the study as they refused therapy and 4 did not complete it. These 6 patients were not included in the analysis.
Participants	Number: 64 Source: Patients referred to the spina bifida centre of the paediatric department "Policlinien Gemelli" of Rome with neural tube defect Inclusion criteria: Spina bifida children with chronic neurogenic constipation aged 3-14 years, defined according to Rome diagnostic criteria. Exclusion criteria: Not stated
Interventions	After initial enema or manual extraction to clean the bowel, patients were randomly assigned to receive either PEG 4000 (0.5g/kg/day) or lactulose (1.5g/kg/day). They were monitored for 6 months and during the trial, doses could only be reduced by the physician if deemed necessary, not increased.
Outcomes	Included in review: None Excluded from review: Bowel frequency as no comparable data available, frequency of encoperesis, resolution of constipation
Notes	Location: "Policlinien Gemelli" Paediatric Department, Rome, Italy Source of funding: No external funding received Attempts to clarify information: attempted to contact authors via email to obtain raw data for comparison. Language of Publication: English

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not stated
Allocation concealment?	Unclear	Not stated
Blinding? All outcomes	Unclear	Not stated
Incomplete outcome data addressed? All outcomes	No	70 patients were randomised, 2 patients did not enter the study as they refused therapy and 4 did not complete it. These 6 patients were not included in the analysis.
Free of selective reporting?	Unclear	Did not report on form of stool, relief of abdominal pain or use of additional products

Rendeli 2006 (*Continued*)

Free of other bias?	Yes	

Voskuijl 2004

Methods	Generation of allocation sequence: Patients were randomly assigned either lactulose or PEG Allocation concealment: Unlabelled numbered boxes with unlabelled sachets prepared by the academic medical centre pharmacy. Blinding: Double blinding Inclusion of all randomised: Yes
Participants	Number: 100 Source: Patients referred by school doctors, GPs and paediatricians to the Department of Paediatric Gastroenterology and Nutritian, Academic Medical Centre, Emma Children's Hospital, Amsterdam, The Netherlands. Inclusion criteria: Children with constipation referred by school doctors, GPs and paediatricians, aged 6 months to 15 years. Childhood constipation was defined as having at least two out of four of the following symptoms for the last three months: less than 3 bowel movements per week, encoperesis more than once a week, large amounts of stool every 7 to 30 days, palpable abdominal or rectal mass. Exclusion criteria: children with organic causes for defecations disorders.
Interventions	Run-in phase, no oral laxatives then one enema per day for three consecutive days. Treatment phase: patients aged between 6 months and 6 years began treatment with one sachet of PEG 3350 (2.95g) or lactulose (6g) per day. Those older than six years were given two sachets of each per day. After one week doses were altered if necessary, or a stimulant laxative added. Patients were followed up for eight weeks.
Outcomes	Included in review: stool frequency Excluded from review: frequency of encoperesis, overall treatment success, adverse events.
Notes	Location: Department of Paediatric Gastroenterology and Nutritian, Academic Medical Centre, Emma Children's Hospital, Amsterdam, The Netherlands. Date: not stated Source of funding: Mediserv BV / Clinical research facilities BV, Schaijk, The Netherlands Attempts to clarify information: None required. Language of publication: English

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Patients were 'randomly assigned' either lactulose or PEG
Allocation concealment?	Yes	Unlabelled numbered boxes with unlabelled sachets prepared by the academic medical centre pharmacy

Voskuijl 2004 (*Continued*)

Blinding? All outcomes	Yes	Double blinded
Incomplete outcome data addressed? All outcomes	Yes	None identified
Free of selective reporting?	Unclear	Did not report on form of stool, relief of abdominal pain and use of additional products
Free of other bias?	Yes	

Wang 2007

Methods	Generation of allocation sequence: Randomised Allocation concealment: Active contract method Blinding: Double-dummy Inclusion of all randomised: 113 cases were randomised, 11 were excluded following randomisation, 5 did not take the medications and 6 were lost to follow-up. 25 children withdrew during the trial, which were not calculated into the PPT
Participants	Number: 191 Source: 7 hospitals across China Inclusion criteria: Bristol Stool Standard aged 8-18 years Exclusion criteria: Children having organic digestive disease or systemic disease
Interventions	Run-in Phase: no other medication for treatment of constipation or other medications affecting GI motion for one week. Treatment Phase: Forlax group - 2 bags (20g/bag) in the morning of for fourteen days. Lactulose group - 15mls per day in the first three days, in the fourth to the fourteenth days, 10mls were taken.
Outcomes	Included in review: Form of stool, relief of abdominal pain Excluded from review: Stool frequency per week, safety evaluation
Notes	Location: Department of Paediatrics, Tangdu Hospital, 4th Military Medical University, Xi-An, China Date: July 2004-March 2005 Source of funding: Not stated Attempts to clarify information: Not required. Language of Publication: Mandarin - Translated to English.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not stated
Allocation concealment?	Yes	Active contract method

Wang 2007 (*Continued*)

Blinding? All outcomes	Yes	Double dummy
Incomplete outcome data addressed? All outcomes	No	113 cases were randomised, 11 were excluded following randomisation, 5 did not take the medication and 6 were lost to follow-up. 25 children withdrew during the trial, which were not calculated into the PPT
Free of selective reporting?	Unclear	Did not report on use of additional products
Free of other bias?	Yes	

Zhang 2003

Methods	Generation of allocation sequence: Randomised, comparative trial. Allocation concealment: Not stated Blinding: Not stated Inclusion of all randomised: 85 patients were recruited but 5 withdrew during treatment
Participants	Number: 85 Source: Department of Gastroenterology, The First Hospital of Quanzhou, Fujian Province, China Inclusion criteria: Aged 60-70 years with constipation for more that three months who, without medicine, pass stool less than or equal to once a week and at least 25% of the time find it difficult to pass stool or pass hard stool and/or strain to pass stool. Exclusion criteria: Colorectal organic disease, faecal occult blood test positive.
Interventions	15mls bd of lactulose or 10g of PEG 4000, into 200mls of water bd, for four weeks. No other medicine for constipation was taken during the trial.
Outcomes	Included in review: Form of Stool Excluded from review: Pass stool times, side effects
Notes	Location: Department of Gastroenterology, The First Hospital of Quanzhou, Fujian Province, China Source of funding: Not stated Attempts to clarify information: None required Language of publication: Mandarin, translated to English.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not stated

Zhang 2003 (*Continued*)

Allocation concealment?	Unclear	Not stated
Blinding? All outcomes	Unclear	Not stated
Incomplete outcome data addressed? All outcomes	No	85 patients were recruited but 5 withdrew during treatment
Free of selective reporting?	No	Did not report on stool frequency, relief of abdominal pain and use of additional products
Free of other bias?	Yes	

Characteristics of excluded studies *[ordered by study ID]*

Brandt 2005	Not a randomised controlled trial
Christie 2002	Not a randomised controlled trial. Used data already presented by Attar 1999 (included in the review) to analyse the economic impact.
Ferguson 1999	Abstract only available. Unsuccessful attempts made to contact authors.
Fritz 2005	Not a randomised study.
Guest 2004	Not a randomised study, this was an economic analysis.
Van der Spoel 2007	Included only patients with acute constipation.

DATA AND ANALYSES

Comparison 1. Stool Frequency per Week

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Stool frequency per week - all comparable data	5	407	Mean Difference (IV, Random, 95% CI)	0.65 [0.15, 1.15]
2 Stool frequency per week - Children	3	227	Mean Difference (IV, Random, 95% CI)	1.57 [0.36, 2.77]
3 Stool frequency per week - Adults	2	180	Mean Difference (IV, Fixed, 95% CI)	0.28 [0.10, 0.45]
4 Stool frequency per week - all comparable data excluding studies to improve heterogeneity	3	280	Mean Difference (IV, Fixed, 95% CI)	0.28 [0.11, 0.45]

Comparison 2. Form of Stool

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Form of Stool - All comparable data	2	301	Mean Difference (IV, Random, 95% CI)	0.89 [0.43, 1.35]
2 Form of Stool - Children	1	216	Mean Difference (IV, Fixed, 95% CI)	0.63 [0.33, 0.93]
3 Form of Stool - Adults	1	85	Mean Difference (IV, Fixed, 95% CI)	1.1 [0.99, 1.21]

Comparison 3. Relief of Abdominal Pain

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Relief of Abdominal Pain - all comparable data	3	300	Odds Ratio (M-H, Fixed, 95% CI)	2.09 [1.26, 3.44]
2 Relief of Abdominal Pain - Children	2	235	Odds Ratio (M-H, Fixed, 95% CI)	2.52 [1.45, 4.40]
3 Relief of Abdominal Pain - Adults	1	65	Odds Ratio (M-H, Fixed, 95% CI)	0.86 [0.25, 2.90]

Comparison 4. Did not require additional products

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Did not require additional products - all comparable data	3	225	Odds Ratio (M-H, Fixed, 95% CI)	4.00 [2.01, 7.95]
2 Did not require additional products - Children	2	126	Odds Ratio (M-H, Fixed, 95% CI)	5.69 [2.06, 15.68]
3 Did not require additional products - Adults	1	99	Odds Ratio (M-H, Fixed, 95% CI)	2.79 [1.07, 7.27]

Analysis 1.1. Comparison 1 Stool Frequency per Week, Outcome 1 Stool frequency per week - all comparable data.

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

Comparison: 1 Stool Frequency per Week

Outcome: 1 Stool frequency per week - all comparable data

Study or subgroup	PEG N	Mean(SD)	Lactulose N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Attar 1999	60	1.3 (0.7)	55	0.9 (0.6)		34.4 %	0.40 [0.16, 0.64]
Bouhnik 2004	32	1.26 (0.65)	33	1.12 (0.33)		34.0 %	0.14 [-0.11, 0.39]
Candy 2006	27	9.4 (4.56)	26	5.9 (4.29)		3.9 %	3.50 [1.12, 5.88]
Gremse 2002	37	14.8 (1.4)	37	13.5 (1.5)		22.5 %	1.30 [0.64, 1.96]
Voskuijl 2004	50	7.12 (5.14)	50	6.43 (5.18)		5.2 %	0.69 [-1.33, 2.71]
Total (95% CI)	**206**		**201**			**100.0 %**	**0.65 [0.15, 1.15]**

Heterogeneity: Tau² = 0.17; Chi² = 17.58, df = 4 (P = 0.001); I² =77%

Test for overall effect: Z = 2.56 (P = 0.010)

Analysis 1.2. Comparison 1 Stool Frequency per Week, Outcome 2 Stool frequency per week - Children.

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

Comparison: 1 Stool Frequency per Week

Outcome: 2 Stool frequency per week - Children

Study or subgroup	PEG N	Mean(SD)	Lactulose N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Candy 2006	27	9.4 (4.56)	26	5.9 (4.29)		18.7 %	3.50 [1.12, 5.88]
Gremse 2002	37	14.8 (1.4)	37	13.5 (1.5)		57.7 %	1.30 [0.64, 1.96]
Voskuijl 2004	50	7.12 (5.14)	50	6.43 (5.18)		23.5 %	0.69 [-1.33, 2.71]
Total (95% CI)	**114**		**113**			**100.0 %**	**1.57 [0.36, 2.77]**

Heterogeneity: $Tau^2 = 0.54$; $Chi^2 = 3.54$, df = 2 (P = 0.17); $I^2 = 44\%$

Test for overall effect: Z = 2.55 (P = 0.011)

Analysis 1.3. Comparison 1 Stool Frequency per Week, Outcome 3 Stool frequency per week - Adults.

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

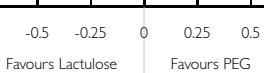
Comparison: 1 Stool Frequency per Week

Outcome: 3 Stool frequency per week - Adults

Study or subgroup	PEG N	Mean(SD)	Lactulose N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Attar 1999	60	1.3 (0.7)	55	0.9 (0.6)		52.9 %	0.40 [0.16, 0.64]
Bouhnik 2004	32	1.26 (0.65)	33	1.12 (0.33)		47.1 %	0.14 [-0.11, 0.39]
Total (95% CI)	**92**		**88**			**100.0 %**	**0.28 [0.10, 0.45]**

Heterogeneity: $Chi^2 = 2.17$, df = 1 (P = 0.14); $I^2 = 54\%$

Test for overall effect: Z = 3.15 (P = 0.0017)



Analysis 1.4. Comparison 1 Stool Frequency per Week, Outcome 4 Stool frequency per week - all comparable data excluding studies to improve heterogeneity.

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

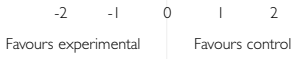
Comparison: 1 Stool Frequency per Week

Outcome: 4 Stool frequency per week - all comparable data excluding studies to improve heterogeneity

Study or subgroup	PEG N	Mean(SD)	Lactulose N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Attar 1999	60	1.3 (0.7)	55	0.9 (0.6)		52.5 %	0.40 [0.16, 0.64]
Bouhnik 2004	32	1.26 (0.65)	33	1.12 (0.33)		46.8 %	0.14 [-0.11, 0.39]
Voskuijl 2004	50	7.12 (5.14)	50	6.43 (5.18)		0.7 %	0.69 [-1.33, 2.71]
Total (95% CI)	**142**		**138**			**100.0 %**	**0.28 [0.11, 0.45]**

Heterogeneity: Chi^2 = 2.32, df = 2 (P = 0.31); I^2 =14%

Test for overall effect: Z = 3.19 (P = 0.0014)



Analysis 2.1. Comparison 2 Form of Stool, Outcome 1 Form of Stool - All comparable data.

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

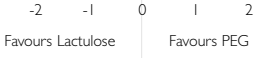
Comparison: 2 Form of Stool

Outcome: 1 Form of Stool - All comparable data

Study or subgroup	PEG N	Mean(SD)	Lactulose N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Wang 2007	105	4.26 (0.89)	111	3.63 (1.33)		45.4 %	0.63 [0.33, 0.93]
Zhang 2003	41	4 (0.3)	44	2.9 (0.2)		54.6 %	1.10 [0.99, 1.21]
Total (95% CI)	**146**		**155**			**100.0 %**	**0.89 [0.43, 1.35]**

Heterogeneity: Tau^2 = 0.10; Chi^2 = 8.31, df = 1 (P = 0.004); I^2 =88%

Test for overall effect: Z = 3.79 (P = 0.00015)



Analysis 2.2. Comparison 2 Form of Stool, Outcome 2 Form of Stool - Children.

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

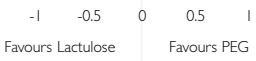
Comparison: 2 Form of Stool

Outcome: 2 Form of Stool - Children

Study or subgroup	PEG N	Mean(SD)	Lactulose N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Wang 2007	105	4.26 (0.89)	111	3.63 (1.33)		100.0 %	0.63 [0.33, 0.93]
Total (95% CI)	**105**		**111**			**100.0 %**	**0.63 [0.33, 0.93]**

Heterogeneity: not applicable

Test for overall effect: Z = 4.11 (P = 0.000039)



Analysis 2.3. Comparison 2 Form of Stool, Outcome 3 Form of Stool - Adults.

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

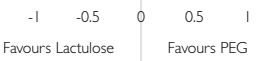
Comparison: 2 Form of Stool

Outcome: 3 Form of Stool - Adults

Study or subgroup	PEG N	Mean(SD)	Lactulose N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Zhang 2003	41	4 (0.3)	44	2.9 (0.2)		100.0 %	1.10 [0.99, 1.21]
Total (95% CI)	**41**		**44**			**100.0 %**	**1.10 [0.99, 1.21]**

Heterogeneity: not applicable

Test for overall effect: Z = 19.74 (P < 0.00001)



Analysis 3.1. Comparison 3 Relief of Abdominal Pain, Outcome 1 Relief of Abdominal Pain - all comparable data.

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

Comparison: 3 Relief of Abdominal Pain

Outcome: 1 Relief of Abdominal Pain - all comparable data

Study or subgroup	PEG n/N	Lactulose n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Bouhnik 2004	26/33	26/32		26.2 %	0.86 [0.25, 2.90]
Dupont 2005	9/11	3/8		3.0 %	7.50 [0.92, 61.05]
Wang 2007	79/105	63/111		70.9 %	2.32 [1.30, 4.14]
Total (95% CI)	**149**	**151**		**100.0 %**	**2.09 [1.26, 3.44]**

Total events: 114 (PEG), 92 (Lactulose)

Heterogeneity: Chi^2 = 3.60, df = 2 (P = 0.17); I^2 =44%

Test for overall effect: Z = 2.88 (P = 0.0040)

Analysis 3.2. Comparison 3 Relief of Abdominal Pain, Outcome 2 Relief of Abdominal Pain - Children.

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

Comparison: 3 Relief of Abdominal Pain

Outcome: 2 Relief of Abdominal Pain - Children

Study or subgroup	PEG n/N	Lactulose n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Dupont 2005	9/11	3/8		4.0 %	7.50 [0.92, 61.05]
Wang 2007	79/105	63/111		96.0 %	2.32 [1.30, 4.14]
Total (95% CI)	**116**	**119**		**100.0 %**	**2.52 [1.45, 4.40]**

Total events: 88 (PEG), 66 (Lactulose)

Heterogeneity: Chi^2 = 1.12, df = 1 (P = 0.29); I^2 =11%

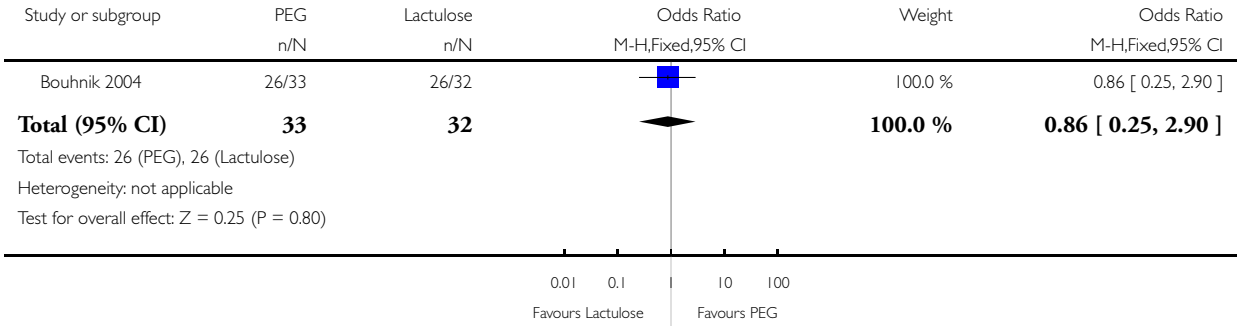
Test for overall effect: Z = 3.26 (P = 0.0011)

Analysis 3.3. Comparison 3 Relief of Abdominal Pain, Outcome 3 Relief of Abdominal Pain - Adults.

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

Comparison: 3 Relief of Abdominal Pain

Outcome: 3 Relief of Abdominal Pain - Adults

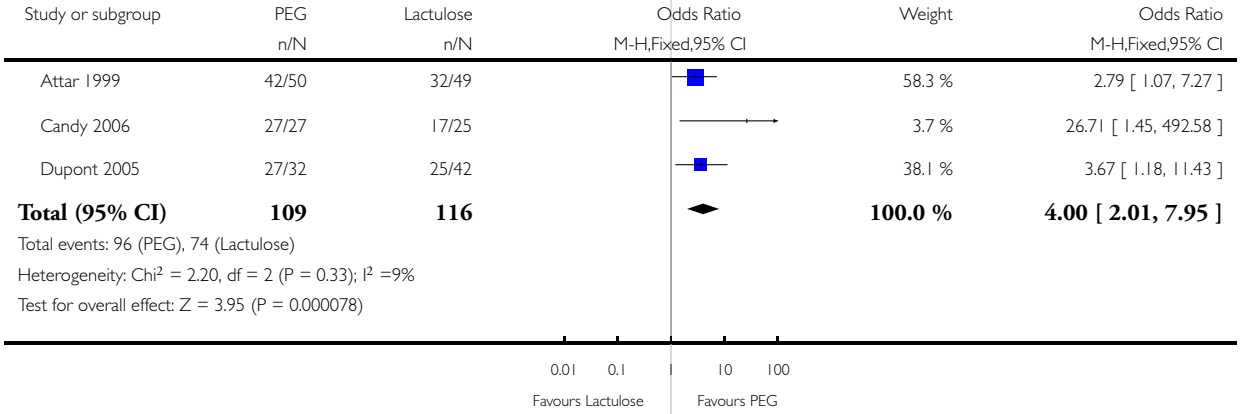


Analysis 4.1. Comparison 4 Did not require additional products, Outcome 1 Did not require additional products - all comparable data.

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

Comparison: 4 Did not require additional products

Outcome: 1 Did not require additional products - all comparable data



Analysis 4.2. Comparison 4 Did not require additional products, Outcome 2 Did not require additional products - Children.

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

Comparison: 4 Did not require additional products

Outcome: 2 Did not require additional products - Children

Study or subgroup	PEG n/N	Lactulose n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Candy 2006	27/27	17/25		8.8 %	26.71 [1.45, 492.58]
Dupont 2005	27/32	25/42		91.2 %	3.67 [1.18, 11.43]
Total (95% CI)	**59**	**67**		**100.0 %**	**5.69 [2.06, 15.68]**
Total events: 54 (PEG), 42 (Lactulose)					
Heterogeneity: Chi^2 = 1.65, df = 1 (P = 0.20); I^2 =39%					
Test for overall effect: Z = 3.36 (P = 0.00077)					

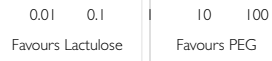
Analysis 4.3. Comparison 4 Did not require additional products, Outcome 3 Did not require additional products - Adults.

Review: Lactulose versus Polyethylene Glycol for Chronic Constipation

Comparison: 4 Did not require additional products

Outcome: 3 Did not require additional products - Adults

Study or subgroup	PEG n/N	Lactulose n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Attar 1999	42/50	32/49		100.0 %	2.79 [1.07, 7.27]
Total (95% CI)	**50**	**49**		**100.0 %**	**2.79 [1.07, 7.27]**
Total events: 42 (PEG), 32 (Lactulose)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.10 (P = 0.036)					



APPENDICES

Appendix 1. Comprehensive Search Strategy

Search strategy for review HLR 057

('Polyethylene glycol versus Lactulose for faecal impaction in patients with chronic constipation')

The Cochrane Library (24.01.08) (41 hits in Clinical trials):

#1 (faecal impaction) or (chronic constipation) or (retention) or (delayed bowel movement) or (obstipation) or (costiveness) or (irregularity) or (feces) or (egest) 8483

#2 MeSH descriptor Constipation explode all trees 544

#3 (#1 OR #2) 8809

#4 4 (Polyethylene glycol) or (ethylene glycol) or (PEG) or (ethylene oxide) or (PEO) or (polyethers) or (laxatives) or (Movicol) or (polyethylene glycol 3350) or (MiraLax) or (GlycoLax) or (GoLYTELY) or (GlycoLax) or (Fortrans) or (TriLyte) or (Colyte) 1644

#5 MeSH descriptor Polyethylene Glycols explode all trees 991

#6 (#4 OR #5) 2124

#7 (lactulose) or (disaccharide) or (Generlac) or (Cephulac) or (Cholac) or (Constilac) or (Enulose) or (cilac) or (Heptalac) or (Actilax) or (Duphalac) or (Kristalose) or (Apo-Lactulose) 677

#8 MeSH descriptor Lactulose explode all trees 230

#9 (#7 OR #8) 677

#10 (#3 AND #6 AND #9) 56 (9 reviews 41 clinical trials)

EMBASE (Webspirs 5.1, Silver Platter version 2.0) (24.01.08) (81 hits)

#28 #10 and #27 81

#27 #22 not #26 1743633

#26 #24 not #25 2733327

#25 #23 and #24 498650

#24 (ANIMAL or NONHUMAN) in DER 3231977

#23 HUMAN in DER 6017497

#22 #19 or #20 or #21 2783097

#21 (SINGL* or DOUBL* or TREBL* or TRIPL*) near ((BLIND* or MASK*) in TI,AB) 88453

#20 (RANDOM* or CROSS?OVER* or FACTORIAL* or PLACEBO* or VOLUNTEER*) in TI,AB 488225

#19 #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 2583416

#18 "SINGLE-BLIND-PROCEDURE"/ all subheadings 7024

#17 "DOUBLE-BLIND-PROCEDURE"/ all subheadings 66374

#16 "PHASE-4-CLINICAL-TRIAL"/ all subheadings 619

#15 "PHASE-3-CLINICAL-TRIAL"/ all subheadings 7693

#14 "MULTICENTER-STUDY"/ all subheadings 40641

#13 "CONTROLLED-STUDY"/ all subheadings 2552498

#12 "RANDOMIZATION"/ all subheadings 24156

#11 "RANDOMIZED-CONTROLLED-TRIAL"/ all subheadings 148911

#10 #3 and #6 and #9 367

#9 #7 or #8 8788

#8 explode "lactulose-" / all SUBHEADINGS in DEM,DER,DRM,DRR 3294

#7 (lactulose) or (disaccharide) or (Generlac) or (Cephulac) or (Cholac) or (Constilac) or (Enulose) or (cilac) or (Heptalac) or (Actilax) or (Duphalac) or (Kristalose) or (Apo-Lactulose) 8788

#6 #4 or #5 44699

#5 (explode "macrogol-" / all SUBHEADINGS in DEM,DER,DRM,DRR) or (explode "polyethylene-" / all SUBHEADINGS in DEM,DER,DRM,DRR) 19335

#4 (Polyethylene glycol) or (ethylene glycol) or (PEG) or (ethylene oxide) or (PEO) or (polyethers) or (laxatives) or (Movicol) or (polyethylene glycol 3350) or (MiraLax) or (GlycoLax) or (GoLYTELY) or (GlycoLax) or (Fortrans) or (TriLyte) or (Colyte)or (macrogol) 38651

#3 #1 or #2 132111

#2 explode "constipation-" / all SUBHEADINGS in DEM,DER,DRM,DRR 23107

#1 (faecal impaction) or (chronic constipation) or (retention) or (delayed bowel movement) or (obstipation) or (costiveness) or (irregularity) or (feces) or (egest) 113506

Medline (Webspirs 5.1, Silver Platter version 2.0) (24.01.08) (32 hits)

#10 and #21 32
#21 #17 not #20 711841
#20 #18 not (#18 and #19) 119606
#19 (humans) in MESH 143
#18 (animals) in MESH 119607
#17 #11 or #12 or #13 or #14 or #15 or #16 713797
#16 trial in TI 74142
#15 randomly in AB 132363
#14 (clinical trials) in MESH 143440
#13 placebo in AB 108575
#12 randomized in AB 173365
#11 clinical-trial in pt 439025
#10 #3 and #6 and #9 79
#9 #7 or #8 7021
#8 explode "Lactulose-" / all SUBHEADINGS in MIME,MJME,PT 1365
#7 (lactulose) or (disaccharide) or (Generlac) or (Cephulac) or (Cholac) or (Constilac) or (Enulose) or (cilac) or (Heptalac) or (Actilax) or (Duphalac) or (Kristalose) or (Apo-Lactulose) 7021
#6 #4 or #5 51704
#5 explode "Polyethylene-Glycols" / all SUBHEADINGS in MIME,MJME,PT 28236
#4 (Polyethylene glycol) or (ethylene glycol) or (PEG) or (ethylene oxide) or (PEO) or (polyethers) or (laxatives) or (Movicol) or (polyethylene glycol 3350) or (MiraLax) or (GlycoLax) or (GoLYTELY) or (GlycoLax) or (Fortrans) or (TriLyte) or (Colyte) or (macrogol) 33579
#3 #1 or #2 159498
#2 explode "Constipation-" / all SUBHEADINGS in MIME,MJME,PT 7121
#1 (faecal impaction) or (chronic constipation) or (retention) or (delayed bowel movement) or (obstipation) or (costiveness) or (irregularity) or (feces) or (egest) 153855

HISTORY

Protocol first published: Issue 1, 2009

Review first published: Issue 7, 2010

CONTRIBUTIONS OF AUTHORS

Draft the protocol (HLR, KT, JM, RLN)

Develop the search strategy (HLR, KT, JM, RLN)

Extract data (HLR, KT, JM)

Data Analysis (HLR, KT, JM, RLN)

Construction of review (HLR, JKT, JM, RLN)

DECLARATIONS OF INTEREST

None

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

N/A

NOTES

Poster presentation at European Society of Coloproctology 4th Annual Meeting, Prague, Czech Republic. 23-26 September 2009.

Colorectal Disease, September 2009; 11 (suppl 2), 29 [Abstract only]