

# A literature review of two laxatives: lactulose and polyethylene glycol

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Constipation is a frequently reported lower gastrointestinal disorder in the community setting, and can be regarded as the passage of hard stools less frequently than the individual's normal pattern (Joint Formulary Committee (JFC), 2011). In order to obtain a diagnosis a bowel assessment must be carried out. This should include a consented digital rectal examination (DRE) (Kyle, 2007). The 'Rome III' criteria form a useful tool in diagnosing chronic constipation (Drossman, 2006). Patients who present with symptoms such as blood, mucus in the stool, constipation alternating with diarrhoea and abdominal pain or vomiting should be referred to their GP (National Prescribing Centre, 1999). Following a diagnosis of constipation, a decision can be made for appropriate intervention.

Laxatives are widely prescribed as a management for constipation (NPC, 1999), and there are many types available. In England in 2006 primary care staff wrote 14.4 million prescriptions for laxatives at a cost of £57.6 million (Information Centre, 2007). The NPF recommends increasing dietary fibre and fluid intake when treating simple constipation (JFC, 2009). However, laxatives may be needed when lifestyle and dietary changes fail to relieve constipation (Bateman and Smith, 1988). Selecting when to use a laxative and which one is appropriate can be a challenge for nurse prescribers. Osmotic laxatives work in one of two ways: either by helping retain fluid in the large bowel, or by drawing fluid from the body into the bowel (JFC, 2011). Two osmotic laxatives, lactulose and polyethylene glycol

(PEG) (also known as macrogols), are commonly used to treat chronic constipation (Bouhnik et al, 2004). The disaccharide lactulose is not absorbed and is partly metabolized by colonic bacteria (Clausen and Mortensen, 1997). It produces a diarrhoea with low pH (JFC, 2011). The polymer PEG retains fluid in the bowel (JFC, 2011). This review explores the literature on two osmotic laxatives, lactulose and PEG, in order to determine appropriate prescribing decisions.

## Lactulose and PEG

Lactulose is considered a pre-biotic contributing to host health (Gibson and Roberfroid, 1995). Lactulose solution, taken orally, up to 15ml twice daily can be prescribed in adults and adjusted dependant on response (JFC, 2011). Lactulose is licensed for constipation.

Macrogol 3350 is the named PEG listed in the BNF (JFC, 2011). Normal dosage is 1–3 sachets daily taken orally for chronic constipation. Up to eight sachets can be used a day for faecal impaction for a maximum of three days. The sachets of PEG are diluted with water, usually 125ml or as instructed by the manufacturer. PEG is licensed for patients who are constipated and faecal impacted.

Contraindications for PEG include intestinal perforation or obstruction, severe inflammatory bowel diseases and paralytic ileus (JFC, 2009). Lactulose has fewer contraindications: galactosaemia and intestinal obstruction. Side effects with PEG include nausea and abdominal distension and pain, while for lactulose they include flatulence, cramps and abdominal discomfort (JFC, 2011).

## Search methods

CINAHL, EMBASE, MEDLINE, and CENTRAL (Cochrane Central Register of Controlled Trials) databases were searched for randomized controlled trials (RCT). Key words such as 'chronic constipation', 'osmotic laxative', 'lactulose', 'polyethylene glycol' and 'macrogols' were used in the search, and combined to narrow results. Nursing databases were consulted but revealed a limited number of RCTs. Thus papers used in this review are mainly from specialist medical journals. NPC bulletins were included to widen the scope on laxatives. Papers identified in a recent systematic review by Lee-Robichaud et al (2010) have been included here. Crombie (1996) recognizes that reviews can be subject to bias and error. It was considered reasonable to undertake an independent review of these papers in order to explore

## ABSTRACT

This paper presents a literature review of two commonly used osmotic laxatives, lactulose and polyethylene glycol (PEG). With increasing numbers of nurses in the community being non-medical prescribers, informed decisions on choice of laxatives is required. Nurses who do not prescribe will often have a view for the benefit of their patients. Following a literature search, eight papers were selected for review. The review leads to the conclusion that, while both preparations are useful, PEG is more effective in many instances and should be the laxative of choice unless there are contraindications arising from the assessment of the patient. Non-pharmacological approaches to the management of constipation should be addressed before considering laxative use.

## KEY WORDS

Constipation ♦ Osmotic laxatives ♦ Review ♦ Lactulose ♦ PEG

them in more depth. Magnesium salts (a type of osmotic laxative) were not included in this review as these are normally used for bowel preparation before surgery (NPC, 1999).

While some of the key pieces of evidence included here might be considered a little out of date, this is owing to lack of recent publications. All included publications are considered relevant. In this review macrogol and polyethylene glycol are referred to as PEG. *Table 1* summarizes the eight studies included in this review.

## Literature review

### Study 1

Attar et al (1999) compared the use of PEG (Movicol) against lactulose. Patient groups were formed randomly to receive two sachets containing either PEG or lactulose. After two weeks patients controlled their own dosing. PEG was shown to be more effective and better-tolerated than lactulose, and patients using PEG demonstrated a higher number of stools. During the last two weeks when patients were free to dose themselves, the number of sachets used was less in the PEG group than the lactulose group.

The study showed good validity as it was an RCT with quantitative data. Patients with colonic disease and concomitant medications were not included. Factors that may affect the validity of these results include the use of suppositories and enemas, which patients still had access to. Reliability was reduced owing to the use of an assessment scale not recognized internationally. The researchers did not report data on form of stool. This study demonstrates that discussion with patient is pertinent when making a prescribing decision. For nurse prescribers, discussion with the patient's GP would be beneficial to ensure appropriate treatment options.

### Study 2

Voskuil et al (2004) compared PEG with lactulose for functional constipation in children. The researchers randomly allocated 100 children aged 6 months – 15 years to receive lactulose or PEG. Doses were administered according to age. Unlike Study 1, there was a run-in phase. Children were not given oral laxatives for one week, and in the final three consecutive days enemas were administered, clearing the bowel. This increases the validity of the results when compared to Attar, as the bowel was already clear and results could not be affected by use of other laxatives prior to the study. Both groups resulted in a significant decrease in encopresis and increase in defecation frequency. The success rate with PEG (56%) was significantly better than lactulose (29%).

Diary entry scores were completed by the patients to record stool quality, and this decreases the reliability of the study. The children were toileted after meals. Enhanced compliance was achieved using gifts and praise. This may have significantly contributed to the decrease in encopresis. In children both lactulose and PEG appear safe and effective.

### Study 3

In Bouhnik et al's (2004) trial, 65 adult participants accepted a week of diet and laxative restrictions, and then were ran-

domly grouped to receive either lactulose or PEG for four weeks. Stools were collected on days 1, 21, and 28 for bacteriological analysis, tested within 4 hours and then frozen. Both lactulose and PEG were shown to be efficacious and well tolerated. PEG was shown to inhibit colonic fermentation rather than demonstrate the beneficial pre-biotic traits that lactulose does. Lactulose was shown to be more beneficial than PEG on colonic flora.

PEG acts on constipation through mechanical cleansing. The consequences of such effects in the long-term are unknown and further study is needed. Participants reported on the number of stools and symptoms such as bloating, flatus, and abdominal pain. These results showed no significant difference between the groups. Of course, this is subjective to patients and might not be the most reliable tool to measure these symptoms. The way in which laxatives work and affect the body should be considered when making a prescribing decision in the community.

### Study 4

DiPalma et al (2000) investigated PEG against a placebo control. A total of 151 randomised participants were selected after a seven-day enrolment period in which bowel movements were documented. Participants were constipated but otherwise healthy. The majority of participants were female, which may not be representative of the population at risk. However, Everhart et al's (1989) outdated American study reported that being female is an added risk factor. DiPalma et al's participants had baseline observations obtained prior to the study, including sigmoidoscopy or colonoscopy, bloods, urinalysis and stool samples. Participants either received 17g PEG or a dextrose powder placebo. The PEG in question, Miralax, was tasteless. Participants recorded their own bowel movement and subjective symptoms such as flatus and cramps.

The results showed a high statistically significant difference in PEG compared to placebo after the two-week period. Participants in the PEG group reported increased number of stools passed in one week. This study used a subjective diary reporting method for collecting data. Subjective data is more liable to poor reliability as it lacks objective measurement of symptoms (Johnson and Closs, 2006). Despite thorough baseline observations, the publishers failed to repeat these observations after the study. The study confirms the safety of Miralax for the short-term treatment of constipation. Long-term use was not studied, and this is an area that would benefit from further investigation.

### Study 5

In Fritz et al's (2005) study of colonic transit, 20 healthy volunteers aged 20–49 were not allowed alcohol or any medication that alters gastrointestinal motility 24 hours before the study. Participants took PEG or lactulose on three consecutive days. Meals were standardized and doses specified by the experimenters. On day 2 participants swallowed a radioactive marker pellet which could then identify colonic transit on scintigraphy. Twenty-five recordings occurred with lactulose and six with PEG. Stools were obtained, tested and analysed.

Table 1. Summary of the literature review findings

Author/date	Aim	Participants	Location	Results	Variables
Attar et al (1999)	To compare the efficacy of PEG and lactulose in chronic constipation	115 adult patients recruited from general and geriatric hospitals	Scotland and France	PEG Group: higher number of stool and lower daily score for straining than lactulose. PEG was shown to be more effective and better-tolerated than lactulose	Poor reliability due to use of unrecognized scoring system. Good validity as patient group similar and excluded constipation secondary to colonic disease verified by colonoscopist
Bouhnik et al (2004)	To assess the effects of lactulose and PEG on the colonic flora in constipation	65 adults from primary care	France	Both lactulose and PEG are effective and well tolerated. Lactulose can be considered a pre-biotic in constipated patients. PEG decreased colonic fermentation in the stool	Diary recorded symptoms. This tool demonstrated poor reliability. No reporting on form of stool
DiPalma et al (2000)	To determine the efficacy and safety of a new laxative (Miralax) PEG against a placebo	151 healthy adults with no chronic colonic conditions (131 female, 20 male)	USA	Confirms the safety and efficacy of Braintree PEG laxative for the short-term treatment of constipation. Increased bowel movement per week, less reported hard stools and less cramping and gas	Diary recorded symptoms. This tool demonstrated poor reliability. Subjective to each individual. High potential for bias from manufacturer as lead researchers worked for manufacturer of laxative
Freedman et al (1997)	To study the tolerance and efficacy of PEG versus lactulose in relieving opiate induced constipation	57 drug-dependent adults on methadone aged 18–50 years	Sinai Hospital, Maryland, USA	Results show that PEG and lactulose produce more 'non-hard' stools than the placebo and control. PEG produced the loosest stool but lactulose had the most adverse effects. PEG also resulted in diarrhoeal stools	This study also fails to use a reliable tool for collection of data as results were subjective to each patient and the scales were poor. Treatment phase not very well explained
Fritz et al (2005)	To study the effects of lactulose and PEG on colonic transit time	20 healthy adults (15 male, 5 female)	Austria	Lactulose accelerates colonic transit. However, at similar stool weight colonic transit is significantly slower with lactulose than PEG	Small sample group. Poor reliability. Good validity in those variables associated with experiment such as meals; medications were standardized across participants
Mimidis et al (2005)	To study the efficacy of PEG in constipated CAPD	24 chronic renal patients on CAPD	Canada	PEG laxative resulted in a dramatic increase in stool frequency, improvement concerning painful defecation, blood and faecal mass. The study confirms the safety and efficacy of PEG laxative for the short-term treatment of constipation	Reliability: good due to Likert scale for recording symptoms; poor due to narrow sample group
Taylor and Guest (2010)	Cost effectiveness of PEG compared to lactulose in chronic constipation in adults in the UK	2000 patients from THIN database	UK, National Health Service	PEG affords the NHS a cost-effective addition to the range of laxatives available for constipation	Resource use was not collected prospectively and patients were not randomized
Voskuijl et al (2004)	To compare PEG with lactulose in paediatric constipation	100 children aged six months to 15 years	Amsterdam	Both lactulose and PEG groups resulted in a significant increase in defecation frequency and decrease in encopresis. PEG however was associated with a significantly higher success rate (56%) than lactulose (29%)	Toilet training and use of praise and gifts to participants for compliance may have contributed to encopresis results. Unrecognized scoring system. Good validity in that bowel was prepared prior to study

Both increased stool weight and faster colonic transit times were linked to higher lactulose dosages. Colonic transit was significantly slower for lactulose than PEG when stool weights were similar.

This study provides an insight into the effects on colonic transit and the doses that need to be considered when making prescribing decisions. In our experience patients often complain of becoming too loose after taking PEG or lactulose. The study has good validity from standardizing of the meals including time intervals, weight of food and observed eating for participants. However, in a study in which metabolism is a crucial factor, it seems unrepresentative to have a sample group comprising largely younger males.

### Study 6

Taylor and Guest (2010) constructed a decision model for managing chronic constipation. Records of 1000 PEG-treated patients were randomly extracted from The Health Independent Network (THIN) database and matched with 1000 lactulose patients. Only 6 months' data for each patient was used in the analysis. The data examined related to hospital admissions, accident and emergency attendances, clinical visits, diagnostic procedures, laboratory tests, and laxative prescriptions. Successful treatments were achieved in 68% of patients given PEG, compared to 60% of patients given lactulose. Patients on lactulose were more likely to attend hospital accident and emergency or outpatient departments, and less likely to have a GP domiciliary visit than PEG patients.

The study found that PEG provided a cost-effective laxative available for constipation, though data was not prospective and patients were not randomized. This study used estimated data and therefore validity is questionable. It is also notable that significantly more of the PEG-treated patients had used laxatives previously than patients given lactulose. Lactulose was frequently used as a first treatment, and this may have affected the conclusions as the severity of constipation may have differed between the groups. The study also noted that prescribing decisions need to be cost-effective to make best use of the NHS budget; the relative costs of treatment should therefore be known to nurse prescribers (NPC, 1999). Drug costs are highlighted in the BNF and NPF.

### Study 7

Mimidis et al (2005) studied the efficacy of PEG in 24 constipated continuous ambulatory peritoneal dialysis (CAPD) patients with chronic renal failure. All patients had previously tried high fibre diet and lactulose with only partial response. A 4-week washout period was undertaken (similarly to Voskuil et al, 2004 and Bouhnik, 2004). Patients were given a diary to record all bowel movements for an 8-week qualifying period. Patients were then given low doses of PEG orally and efficacy and tolerance were monitored, including number and consistency of stool on a scale of 1–5; pain, rectal irritation, flatus and blood were also recorded.

PEG laxative resulted in a dramatic increase in stool frequency, improvement concerning painful defecation, blood and faecal mass. Only mild changes with cramping flatus and

rectal irritation were noted. The study confirms the safety and efficacy of PEG laxative for the short-term treatment of constipation. The reliability of this study is improved due to use of a Likert-type scale for reporting symptoms and stool consistency. However, the small sample may not be representative of the population of people with constipation. The paper was brief with little in-depth analysis of results. Participants with constipation secondary to colonic disease were excluded. Perhaps the participants should have undergone further investigation, such as colonoscopy, like DiPalma et al's (2000) study to increase validity of results. This study does, however, indicate safe use of PEG with patients in renal failure, a common condition in community practice with the elderly.

### Study 8

Freedman et al's (1997) study was of 57 drug-dependent men and women involved in a methadone maintenance programme who had complained of constipation and had sought the use of laxatives. The study focused on the efficacy and tolerance of lactulose and PEG in resolving opiate-induced constipation. Following a control week during which patients received no treatment, there were three treatment phases each lasting two weeks. Treatments included placebo (water), lactulose diluted in water and PEG. Participants reported stool frequency, stool type, relief from abdominal pain, and use of alternative laxatives. Results showed that PEG and lactulose produced more 'non-hard' stools than the placebo and control. PEG produced the loosest stool but lactulose had the most adverse effects. PEG also resulted in diarrhoeal stools but dose level may have affected this. This study failed to use a tool for data collection that was tested for reliability; results relied on subjective reporting. Treatment phases were not clearly explained. However, the study is useful in practice as in the community IVDU (intravenous drug users) on methadone programmes are frequently treated by the community nurse. Constipation is a frequent issue, and this study demonstrates a safe and effective use for both lactulose and PEG when considering a prescribing decision for short-term constipation.

## Discussion

Some of the trials included in this review were sponsored by drug companies: Bouhnik (2004) was sponsored by Solvay Pharma, DiPalma et al (2000) received a grant and PEG from Braintree Laboratories, and in addition DiPalma serves as a medical director to Braintree Laboratories. The potential for sponsorship bias exists.

Recommendations for further research have been identified from the weaknesses across all the studies included. One major issue is a failure to use a well-recognized tool for assessing stool, such as the Bristol Stool Chart (Heaton and Lewis, 1997). Used across the UK, this tool standardizes nurses' assessment of bowels and stools and may increase the validity and comparability of results. The second recommendation, emerging from Fritz et al (2005) and Attar et al (1999), is that dosing needs to be patient-specific as this may decrease adverse effects such as diarrhoea stools.

This review has shown PEG and lactulose to be safe and effective at treating both short-term and chronic constipation in a range of patient groups. PEG appears more effective than lactulose for improving stool frequency, stool type and abdominal pain relief. In our experience, prescribing patterns in practice suggest that lactulose is favoured by GPs over PEG. This may be due to familiarity with the product.

With both lactulose and PEG available on FP10, a number of community nurses can make a prescribing decision for short-term constipation. Where chronic constipation is concerned, discussion with the patient's GP would be advisable before making a decision, as the patient may benefit from a full medical review. This may highlight whether the constipation is primary (simple or idiopathic), secondary (results from physiological disease or conditions), or iatrogenic (induced from medication or treatment) (Clinical Knowledge Summaries, 2007). By liaising with the GP, amendments to the patient's current medication or treatment (if any) may help to prevent or reduce constipation.

## Conclusion

The key point emerging from this literature review is that both lactulose and PEG are safe and effective to use in constipation (Voskuil et al (2004) and Bouhnik et al (2004)). PEG appears better than lactulose for improving stool frequency, stool type and abdominal pain relief (Freedman et al, 1997; Attar et al, 1999; DiPalma et al, 2000). PEG is shown to be effective in CAPD patients (Mimidis et al, 2005). There is limited evidence to indicate the best economic outcome, although Taylor and Guest's (2010) study concludes that PEG is a cost-effective addition to laxative prescribing. Finally, Bouhnik et al (2004) found that lactulose does show benefit on colonic flora, and the long-term effects of lactulose *versus* PEG need to be addressed. Lactulose also appears to be associated with slower colonic transit when compared to PEG on equal stool weight (Fritz et al, 2005).

It is apparent that there is need for further research concerning the long-term implications of PEG as highlighted by Bouhnik et al (2004). The use of a more reliable tool for obtaining data, like the internationally recognized Bristol Stool Chart (Heaton and Lewis, 1997), might help with reliability of future studies.

In the community when making a prescribing decision, PEG may be an appropriate choice of laxative to use. Several factors should be considered when making the diagnosis, therefore use of medical advice is paramount if there is any doubt in regards to a prescribing decision or diagnosis. A prescription is not always needed. Dietary fibre and fluids

(2 litres per day) can be useful in prevention and treatment (NPC, 1999). In elderly, impacted or immobile patients this can be difficult due to numerous factors including comorbidities, opioid-induced constipation and the increased risk of faecal incontinence (Norton, 1996). In such cases a laxative might be appropriate, although long-term laxative use should be avoided (NPC, 1999). Other factors not addressed include social causes for constipation, which in the elderly can be associated with incontinence prevention; patients may be embarrassed by their faecal incontinence and by constipating themselves episodes of incontinence are reduced. Therefore it is paramount that when making a bowel assessment the patient is viewed holistically.

The literature shows that while PEG and lactulose are both effective, safe and cost-effective to prescribe in both constipation and chronic constipation, PEG appears to be more effective.

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## LEARNING POINTS

- ♦ Lactulose and polyethylene glycol (PEG) are two osmotic laxatives that are effective for the management of constipation
- ♦ PEG appears to be more effective when compared to lactulose
- ♦ A nurse should undertake an assessment of a patient's bowel habits and lifestyle, and consider non-pharmacological approaches to the management of constipation before deciding to prescribe a laxative